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LETTERER-SIWE'S DISEASE

SPLENOHEPATOMEGALY ASSOCIATED WITH WIDESPREAD HYPERPLASIA OF NONLIPOID-STORING MACROPHAGES; DISCUSSION OF THE SO-CALLED RETICULO-ENDOTHELIOSES

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In reviewing the literature in an attempt to identify the condition in the case which we are here reporting, we have found that Letterer,[1] in 1924 under the title "Aleukämische Retikulose (Ein Beitrag zu den proliferativen Erkrankungen des Retikuloendothelialapparates)," described the occurrence of splenohepatomegaly, associated with anemia, and a purpuric eruption in a 6 month old infant. The child died four days after admission to the hospital, and at autopsy the histologic examination revealed a unique and surprising condition. In the liver, spleen, lymph nodes, bone marrow and skin there was a proliferation of large, pale reticulo-endothelial cells, invading and replacing the normal structure of these organs.

Following the publication of Letterer's article, several quite similar cases were reported, but it was not until 1933 that Siwe,[2] in describing a similar case in a 16 month old infant in an article entitled "Die Reticuloendotheliose—ein neues Krankheitsbild unter den Hepatosplenomegalien," grouped the previously reported cases with his own into a well defined clinical pathologic entity.

We have therefore chosen the title "Letterer-Siwe's Disease" as an appropriate designation for this group of cases.

According to Siwe's criteria, the condition is characterized by the following distinctive features:

1. There is marked splenomegaly, with from moderate to considerable enlargement of the liver.

From the Sarah Morris Hospital for Children, Michael Reese Hospital.

1. Letterer, E.: Aleukämische Retikulose, Frankfurt. Ztschr. f. Path. **30**: 377, 1924.

2. Siwe, S.: Die Reticuloendotheliose—ein neues Krankheitsbild unter den Hepatosplenomegalien, Ztschr. f. Kinderh. **55**:212, 1933.

2. A hemorrhagic tendency, chiefly manifested as petechiae or purpura, has consistently been noted.

3. There is a generalized enlargement of the lymph glands. The glands are discrete and not tender.

4. Localized tumors over the bones may be present. The osseous involvement, however, may be recognized only by the aid of roentgenograms or at autopsy.

5. The blood picture is characterized by secondary anemia of a progressive, nonregenerative type. The leukocyte count is normal or somewhat diminished. The differential count is within normal range, and in none of the cases was there a marked increase in the percentage of mononuclears. The number of platelets, in those instances in which they were reported, was not consistently diminished.

6. Splenic puncture may reveal an increased number of nonlipoid-containing macrophages.

7. The disease is neither of a hereditary nor of a familial character, and it occurs exclusively in infants. The onset is acute and is unrelated to infection. The course is gradually downhill, and the duration of the disease has varied from a few weeks to several years. The etiology is unknown.

8. The pathologic changes are characterized by a generalized hyperplasia of the macrophages in various organs. These cells are nonlipoid-storing. The characteristic cells are large, round or polygonal mononuclear cells. The cytoplasm is pale-staining; the nucleus is usually chromatic, often eccentrically situated, in some instances vesicular in shape and in others more oval or spindle-shaped. The cells are nonlipoid-containing. Occasional giant cells, some of which are multinuclear, have been noted. A definite increase in the reticular fibers can be demonstrated. The organs chiefly involved are the spleen, liver, lymph glands, bones, lungs, skin, thymus and lymph follicles of the intestine. Notably in the spleen and lymph glands, the presence of the large cells causes a distortion of the normal architecture, and frequently areas of necrosis and hemorrhage have occurred. The involvement of the bone has resulted in cyst or tumor formation.

On the basis of the following case, which we have found to coincide in all details with the clinical and pathologic criteria of Siwe, we wish to discuss the relationship of this condition to the so-called reticulo-endothelioses.

REPORT OF CASE

Clinical History (from the pediatric service of Dr. Mark Jampolis and Dr. I. Harrison Tumpeer).—G. L., a white boy 2 years old, was admitted to the hospital on May 7, 1934, with a complaint of swelling of the left side of the head for six weeks. Four months before entry the patient fell, striking the left side of his head, and for four days following this injury a swelling with some pain was noted at the injured site. He was then entirely well until six weeks before admission, when a

small, hard, nontender swelling appeared on the left side of the head. This swelling became progressively larger and softer, until it reached the size of half an orange. Along with this, however, there had been no change in the child's general appearance or behavior.

The past history revealed that he had an infected nevus over the frontal area of the skull, in the region of the anterior fontanel, which was treated with carbon dioxide snow.

Physical Examination.—The child was well developed and well nourished and not acutely ill. Over the left temporoparietal area, there was a large, soft, fluctuant, nontender, definitely pulsating swelling; the overlying skin was unaffected, and around the edges of the swelling the rough borders of an apparent underlying bony defect were palpable. When the patient cried, the mass became tense. Seborrheic scales were present on the scalp about the swelling. Over the midline frontal area, there was a rectangular white patch 4 by 6 cm. with a pink periphery. This was the scar from the treated nevus.

The spleen was palpable 2 cm. below the left costal arch, and the liver was not palpable. The posterior cervical and inguinal glands were slightly enlarged.

The results of examinations of the blood are shown in table 1. Roentgen examination revealed an irregularly round defect in the left parietal area, about 6.5 cm. in diameter, surrounded by bone of apparently increased density. "The soft tissue swelling occupies a greater area than does the bony defect, giving the impression that the process started superficially rather than from within the skull." The roentgenograms of the chest showed exaggerated hilar and pulmonary markings. The long bones showed no abnormal changes. There was no Bence-Jones protein in the urine. The Wassermann and Mantoux tests gave negative results. The fundi were essentially normal, with "slight peppery distribution of the pigment within normal limits." One week after entry, a loud bruit was heard over the mass on the head, and transillumination, by Dr. Max Cutler, revealed a complete opacity over the area of the tumor. Aspiration of the tumor was attempted, though this yielded only a small amount of blood, which microscopically showed only red blood cells.

During his stay in the hospital, the patient had frequent periods of fever (temperature from 101 to 102 F.). The spleen became larger and the liver distinctly palpable; petechiae developed in both inguinal regions. Two weeks after entry (May 21) radium pack therapy was instituted, and on May 26 the tumor was smaller and less pulsatile, though the liver and spleen increased greatly in size, both reaching to the iliac crests. He was discharged on May 26, to be followed in the outpatient department and to receive continued radium therapy.

He was readmitted to the hospital on June 5, after daily radium treatments. Examination at this time revealed moderate pallor, marked splenohepatomegaly, large axillary and moderate cervical and inguinal adenopathy and petechiae over the elbows, neck and inguinal regions. The tumor on the head had not changed in size. The blood counts are noted in table 1. Repeated roentgenograms of the skull, long bones and vertebrae revealed no appreciable change from the last examination.

The subsequent course was rapidly downhill, despite blood transfusions and radium therapy. The mass on the head increased in size, and on June 29 radium therapy was discontinued, because of the anemia and leukopenia. Splenic puncture was done, though microscopic examination showed only splenic pulp cells and normal blood. The temperature reached from 101 to 104 F. daily for two weeks before death occurred, and during this time massive showers of petechiae, some of which appeared to be definitely elevated above the surrounding skin, developed and

extended over the entire body, being especially prominent on the abdomen, head, hands and feet. Ecchymoses were also noted. The patient lost ground daily and died on July 26, four and one-half months after the onset of the illness.

Autopsy was performed about one hour after death (service of Dr. Otto Saphir).

Macroscopic Examination at Necropsy.—External Examination: The body was that of a fairly well developed, moderately well nourished boy about 3 years old. There was marked edema of the eyelids and cheeks and of the back, abdomen and lower extremities. The scrotal sac was enlarged and apparently filled with fluid. Many petechial hemorrhages were present over the skin of the chest, abdomen, arms, palms and face. They measured up to 6 mm. in diameter. The conjunctivae, buccal mucosa and skin were very pale. There was a tumor mass which arose in

TABLE 1.—*Data on the Results of Examinations of the Blood of a Patient with Letterer-Siwe's Disease*

Date	Erythrocytes, per Cu.Mm.	Hemoglobin, %	Platelets, per Cu.Mm.	Leukocytes, per Cu.Mm.	Poly. Neutrophils, %	Poly. Eosinophils, %	Poly. Basophils, %	Lymphocytes, %	Monocytes, %	Bleeding Time, Minutes	Coagulation Time, Minutes	Myelocytes, %
5/ 8/34	3,540,000	50 plus	.....	4,950	46	..	..	44	8	..	..	2
5/15/34	3,200,000	60	.....	4,600	65	..	..	32	2	..	..	1
5/18/34	.....	..	.....	3,800	..	..	..	..	..	..	..	..
5/23/34	3,400,000	50	.....	6,200	54	..	..	38	4	..	..	4
6/ 6/34	3,080,000	50	342,000	2,550	58	2	..	42	..	3	6	..
6/10/34	3,240,000	70	.....	3,100	54	..	..	44	2	..	..	..
6/18/34	2,730,000	60	.....	2,700	..	..	..	..	..	..	..	..
6/28/34	3,060,000	..	.....	2,800	50	..	..	46	4	..	..	..
7/ 2/34	.....	..	.....	2,400	..	..	..	..	..	..	..	..
7/ 3/34	2,090,000	40–50	.....	.....	..	..	..	..	..	..	..	..
7/11/34	1,660,000	30–40	.....	2,000	..	..	..	..	..	1¾	2	..
7/12/34	2,310,000	40–50	.....	1,200	52	..	..	48	..	..	..	..
7/14/34	2,130,000	40–50	.....	2,600	..	..	..	..	..	..	..	..
7/16/34	1,940,000	30–40	.....	1,900	..	..	..	..	..	..	..	..
7/18/34	.....	..	.....	1,800	68	..	..	30	2	..	..	..
7/21/34	2,080,000	40–50	.....	1,250	56	..	..	44	..	..	..	..
7/23/34	1,740,000	40	.....	2,100	59	..	..	40	1	..	..	..
7/25/34	1,170,000	30	.....	2,800	..	..	..	..	..	..	..	..
7/26/34	.....	..	.....	3,000	..	..	..	..	..	..	..	..

the region just above the left ear and extended anteriorly to the region of the forehead up to the left orbit. It measured 3 by 10 cm. in diameter and was of semifluctuant consistency. It was covered by skin which was of a purplish color. The tumor could not be moved from the underlying bone, which seemed much thinner than the surrounding bony structures. The skin over the tumor was freely movable. The inguinal, axillary and cervical lymph nodes were enlarged and of soft consistency.

Internal Examination: The skin on section was of normal elasticity. The subcutaneous fat tissue was dark yellow and measured about 3 mm. in thickness. The subcutaneous tissue was moist. The pleural cavities contained a small amount of clear yellow fluid. The surfaces were smooth and glistening. There were no adhesions. The surfaces of the pericardium and peritoneum were smooth and glistening. There were no adhesions. The mediastinal, peritoneal and retroperitoneal lymph nodes were enlarged, measuring 1 cm. in diameter. They were pale pink and soft and revealed a yellowish-red jelly-like cut surface.

The heart weighed 70 Gm. There were petechial hemorrhages on the pericardial surface. The valvular apparatus was intact. The foramen ovale was patent. The myocardium was pale, the architecture indistinct and the cut surface of boiled appearance. The endocardium showed no change. The aorta and coronary vessels appeared normal.

Both lungs weighed 280 Gm. They were pale gray and subcrepitant. On cut section, the surfaces were moist. A moderate amount of a reddish-white fluid could be expressed. Grossly there was no evidence of pneumonia. The hilar lymph nodes were enlarged and reddish and of soft consistency.

The liver was markedly enlarged and weighed 900 Gm. It was of rather soft consistency and pale yellow. On section the architecture was slightly obscured. The central zones, as far as could be made out, were red and depressed and surrounded by a rim of yellow. The periportal spaces were gray. The gallbladder contained a small amount of thin liquid bile. The bile passages showed no changes.

The spleen weighed 375 Gm. and measured 5 by 9 by 16 cm. in diameter. It was of firm consistency and purplish red and revealed a smooth surface. On cut section, the architecture was indistinct. Only outlines of trabeculae were visible. The pulp was purplish red and contained a few yellow, undefined areas measuring up to 5 mm. in diameter. The pulp could not be scraped away with the knife.

Both kidneys weighed 130 Gm. The capsule stripped with ease, revealing a smooth surface. The organ cut with normal resistance. On section the architecture of the cortex was preserved. The boundary between cortex and medulla was not sharp. The pelves, ureters and urinary bladder showed no changes.

With the exception of a moderate amount of fluid within the scrotal sac, the genitalia showed no changes.

The pancreas and adrenals appeared normal.

The mucosa of the entire gastro-intestinal tract was very pale. There was no evidence of inflammation or tumor.

The skull appeared normal with the exception of the area of tumor previously described. When the skull was removed, it was seen that the tumor apparently arose from the outer surface of the dura and had eroded the frontal and temporal bones and extended into the subcutaneous tissue. On section the tumor was dark red, appeared spongy and contained a number of yellowish nodules measuring up to 1.5 cm. in diameter. The tumor was, in many portions, hemorrhagically discolored and showed large areas of necrosis. The inner lining of the dura showed a few areas of hemorrhage but no tumor growth. The left frontal and temporal lobe of the brain in the region of the tumor were compressed. Multiple sections of the brain showed no changes of note.

Only the bone marrow of the ribs could be examined. It was pale red and finely granular and seemed abundant.

Microscopic Examination at Necropsy.—Extradural Tumor Mass: The bulk of this mass consisted of cells which were well defined and showed pink-stained cytoplasm which was partly smooth and partly finely granular. Many of the cells were round or oval; however, they varied somewhat in shape and size. The nuclei were hyperchromatic, often eccentrically situated and distinctly vesicular. Occasionally multinucleated cells were seen in which the nuclei were distributed predominantly within the center of the cells. In other fields areas of fibrosis were prominent. In many sections much reddish-brown, finely granular pigment was seen, partly free in the tissue and partly within the cytoplasm of phagocytic cells. In some sections the cellular area seemed surrounded by a capsule of hyalinized connective tissue, but in other sections there was no sharp demarcation

between the tumor and the surrounding structures. Sections which were stained according to Foote's reticulum stain revealed a delicate network of reticular fibers, which in many instances surrounded the individual cells. The stroma revealed a number of small-sized blood vessels.

Lungs: A number of sections showed the alveoli filled with large cells which were similar in many respects to those seen in the extradural mass just described. The cytoplasm was stained a pale pink. The nuclei were vesicular and hyperchromatic. Whereas most of the cells were noted within the alveoli, they were also present in the perivascular and peribronchial spaces. Occasionally multinucleated cells were seen.

Liver: The liver cells of the periportal spaces contained large fat globules. In many instances the fatty infiltration extended up to the central zones. The sinusoids contained a number of large pale-staining cells similar to those in the tumor.

Spleen: There was a marked increase in connective tissue. The distinction between pulp and follicles was not marked, and throughout the pulp many large cells were seen with eccentrically situated nuclei. Their cytoplasm was faintly eosinophilic and smooth. A number of lymphocytes and plasma cells and a few polymorphonuclear leukocytes were also seen throughout the pulp.

Mesenteric Lymph Nodes: The normal architecture was obscured. Throughout the sinuses many large cells were observed, some of which were similar to those seen within the epidural mass described. Other cells showed only a small amount of cytoplasm surrounding a densely stained nucleus (lymphoblasts). Occasionally multinuclear cells were present. A moderate amount of reticulum was seen throughout the lymph nodes.

Bone Marrow: In addition to nucleated red cells and myeloblastic cells, a number of large cells similar to those described within the epidural mass were present. Occasionally megakaryocytes could be made out.

Sections of the heart, kidneys, pancreas and adrenals revealed no noteworthy histologic changes.

DIFFERENTIAL DIAGNOSIS

Points of special interest in the case described may be noted. The onset was insidious in a previously apparently normal 2 year old child. No familial or hereditary history of the condition was elicited. No relationship could be drawn between the illness described and any previous infection. The most striking point in the infant's appearance at first inspection was the tumor mass on the head. The history contained a statement to the effect that the child sustained a slight injury to the head three months before the tumor was first definitely noted, but we cannot plausibly ascribe to this trauma any etiologic significance. The child did not appear acutely ill on the first admission, and the pulsating tumor on the head, combined with moderate anemia, leukopenia, enlargement of the spleen and a moderate continued rise in temperature, presented a puzzling diagnostic problem. Our first clinical impression was that the condition was a malignant form of hemangioma—a hemangioendothelioma. This diagnosis was particularly influenced by the fact that over the frontal area of the head a coin-sized scar was noted. On questioning the parents, it was ascertained that a vascular nevus had

been present and that this had been treated with carbon dioxide snow. After making laboratory and roentgen examinations, we were particularly impressed by the large defect in the skull and by the leukopenia with the normal differential blood count. These facts rather suggested a lipoid disturbance of the Hand-Schüller-Christian type. However, on splenic puncture, no lipoid-containing cells were found. As we watched the course of the disease and noted the increasing anemia with persistent leukopenia, the continued fever and the increase in the size of the liver and spleen, together with the hemorrhagic tendency, as manifested by crops of petechiae and larger ecchymoses, we concluded that the condition, clinically, closely resembled aleukemic leukemia, with leukemic tumor formation. From examination of the blood, as the blood cells were normal, we were unable to state with which cell type of leukemia we were dealing. The gross pathologic examination gave little additional information, and it was not until a histologic examination was made that we became aware of the probable nature of the condition.

REVIEW OF CASES REPORTED

As previously noted, Siwe collected and reviewed the cases reported up to 1933. He analyzed four cases in his series, including his own (cases 1, 2, 3 and 5). We noted that he overlooked a case reported by Podovinec and Terplan [3] in 1931. Following the criteria of Siwe, we reviewed the literature and were able to find eight previously reported cases. To this we add our own, the ninth reported case. Table 2 contains a detailed analysis of these nine cases.

It will be noted that the youngest patient at the onset of symptoms was 3 months of age and the oldest was 2¾ years. There were three male and five female infants; in Guizetti's [4] case the sex was not stated. In all instances the spleen was definitely enlarged, reaching in its maximum size to the anterior iliac spine. The enlargements of the liver that were noted varied from 2 to 5 fingerbreadths below the costal margin. There was enlargement of the lymph nodes in every case described, except in the case reported by Gittins,[5] who stated that enlargement of the lymph glands was never noticeable. Petechial and ecchymotic cutaneous eruption were present in all cases. The osseous changes were of various nature. The case reported by us was the only one in which a definite tumor was involved. As for the cases reported

3. Podovinec, E., and Terplan, K.: Zur Frage der sogenannten akuten aleukämischen Retikulose, Arch. f. Kinderh. **93**:40, 1931.

4. Guizetti, H. U.: Zur Frage der infektiös bedingten Systemerkrankungen des reticuloendothelialen Apparates im Kindesalter, Virchows Arch. f. path. Anat. **282**:194, 1931.

5. Gittins, R.: Anemia and Reticulo-Endotheliosis, Arch. Dis. Childhood **8**: 367, 1933.

TABLE 2.—*Analysis of Nine Reported Cases of Splenohepatomegaly Associated with Widespread Hyperplasia of Nonlipoid-Storing Macrophages*

Case number	1	2	3	4	5	6	7	8	9
Author	Letterer[1]	Akiba[6]	Guizetti[4]	Podovinec and Terplan[3]	Siwe[2]	Gittins[5] (Case 4)	Foot and Olcott[7]	Roussy and Oberling[8]	Abt-Denenholz
Date	1924	1926	1931	1931	1933	1933	1934	1934	
Age and sex of patient	6 months; boy	10 months; girl	3 months	1 year; girl	16 months; girl	1 year and 11 months; boy	2¾ years; girl	8 months; girl	2 years; boy
Spleen	Large, hard tumor	Distinctly palpable	Several finger-breadths below costal arch	4 fingerbreadths below costal arch	Reached to iliac spine	Enlarged 3 inches; larger later	Enlarged	3 fingerbreadths below costal arch	3 cm. below costal arch; gradually increased to reach umbilicus
Liver	2 finger-breadths below costal arch	.....	2 to 3 finger-breadths below costal arch	4 finger-breadths below costal arch	2 finger-breadths below arch	Gradually enlarged	7 cm. below costal arch	Slightly swollen	Enlarged to reach 5 finger-breadths below costal arch
Lymph nodes	Generalized, with overlying skin reddened	.....	.....	Generalized	Generalized	Never noticeable	Inguinal, posterior and cervical lymph nodes moderately enlarged	Axillary nodes moderately enlarged	Generalized
Cutaneous manifestations	Petechiae and purpura over entire body	Petechiae and purpura	Petechiae over buttocks, bones, mouth and tongue	Petechiae over thorax, trunk and back	Petechiae over back, feet, forearms and axillae	Petechiae and ecchymoses often observed	Body covered with tiny petechiae; showers of petechiae during course	Purpura in hands, gradually spread over entire body; small red flecks, surface over which was desquamating	Generalized petechial and purpuric eruption; showers of petechiae
Osseous changes	None found clinically	None found clinically	Cystic areas found in right humerus on roentgen examination	None found clinically	Cystic areas found in left fibula on roentgen examination	None found	Rarefaction of lower pelvis and right femur near its head; osteoporosis of spine found on roentgen examination	None found	Pulsating tumor over head with large cystic area in bone found on roentgen examination
Fever	Constant for three weeks	Continued fever	Continued fever	Present before and on admission	Continued fever	Rises in temperature occurred with increasing frequency	Subfebrile; average temperature 37.6 C. (99.8 F.)	Moderate fever temperature 38.6 C. (101.6 F.)	Continued fever
Blood findings on admission									
Red blood cells, per cu. mm.	5,600,000	.....	3,000,000	3,300,000	2,400,000	2,500,000	3,700,000	4,100,000	3,540,000
Hemoglobin, %	65 (Sahli)		10.2 Oxy-Hb.	60 (Sahli)	40 (Sahli)	37	75	36 (Sahli)	50 (Talquist)
White blood cells, per cu. mm.	26,000	.....	15,300	13,000	12,500	11,300	3,900	10,000	4,950
Differential count %									
Polymorphonuclears	65	.....	44	49	64	47	39	16	48
Lymphocytes	25		46	47	26	53	39	75	44
Monocytes	8		9	4	10	..	4	9	8
Undifferential count, %	2	.....	.....	.....	.....	.....	.....	.....	.....
Platelets, per cu. mm.	Not diminished	.....	.....	140,000	1,408,000	Decreased to 10,000	120,000 80,000	.....	342,000
Blood culture	.....	.....	.....	.....	No growth	.....	.....	Negative	Negative
Mantoux test	.....	.....	.....	.....	Negative reac-	Negative reac-	.....	.....	Negative reac-

Monocytes	8		9	4	10	..	4	9	8
Undifferential count, %	2	.....	.....	.....	.....	.....	.....	.....	.....
Platelets, per cu. mm.	Not diminished	.....	.....	140,000	1,408,000	Decreased to 10,000	130,000 80,000	.....	342,000
Blood culture	.....	.....	.....	.....	No growth	.....	.....	Negative	Negative
Mantoux test	.....	.....	.....	.....	Negative reaction to 1 mg.	Negative reaction	.....	.....	Negative reaction
Wassermann tests	.....	.....	.....	.....	.....	.....	.....	.....	Negative reaction
Duration	11 weeks	6 weeks	3 weeks	2 weeks	4 months	2 years	1½ years	1 month	4½ months
Author's clinical impression	Sepsis with purpura	Sepsis with ulcerative angina, purpura, and enteritis	Sepsis, osteitis fibrosa in the right humerus	Acute aleukemic lymphadenosis	Septicemia with focus in the left fibula	Aplastic anemia	Nonlipoid histiocytosis (splenic biopsy)	Symptomatic purpura on basis of infection	Aleukemic leukemia with leukemic tumor
Liver	Diffuse fatty changes; infiltration of large, pale cells	High grade fatty changes; groups of cells with necrosis as in glands and spleen	Marked fatty changes, infiltration of large cells often in groups	Marked fatty changes, infiltration of round cells and occurrence of giant cells in capillaries	Marked infiltration of fat in liver cells; Kupffer cells swollen; no giant cells; no necrosis	Marked fatty degeneration in central areas of lobules; many nuclei and cells of all shapes; free histiocytes	Large amount of fat in parenchyma; interlobar fibrosis; some erythrophagocytosis	Diffuse and very marked fatty infiltration; proliferation of reticular elements; central necrosis	Marked fatty changes; many cells completely replaced by fat; in sinusoids many large, pale cells; some multinuclear
Spleen	Absence and distortion of follicles; infiltration of large, pale cells in pulp and sinusoids	Lymph elements reduced; peculiar large cells in groups, irregular with necrotic centers	Marked proliferation of large cells; increase in reticulum; follicles small and infrequent	Follicles partially gone; infiltration with pale, large tumor cells; small areas of necrosis	Large, pale cells in strands or accumulations; numerous mitoses; connective tissue not increased	Lymphocytes in follicles much diminished; extensive collections of large, pale cells; increased reticulum	Sinus and pulp inundated with large polyhedral cells; increase in reticular fibers	Disappearance of follicles; diffuse growth of large cells with hemorrhage and secondary focal necrosis	Distinct increase in connective tissue; architecture obscured; many large, pale cells in pulp and sinusoids
Lymph nodes	Proliferation of reticular cells; supplanting lymphatic tissue	Groups of cells as in spleen	Same infiltration of large cells	Disarrangement of structure; infiltration with pale, large tumor cells; small areas of necrosis	Proliferation of large, pale, polygonal cells; small areas of necrosis	Lymph follicles diminished; striking increase in reticulum and reticulum cells	Sinuses filled with large mononuclear cells; actively phagocytizing erythrocytes	Same picture as the spleen	Architecture completely obscured; large cells throughout sinuses
Bone marrow	Nests of large, pale cells, rich in reticular cells	.....	Masses of typical large cells in marrow; proliferation of reticulum; destruction of lamellae	Proliferation of reticulum cells; phagocytosis of red cells; diminution of myeloid elements	Beneath cystic area bone marrow normal	Increase of pale reticulum cells in same areas; bundles of fine reticular fibers	Phagocytosis of erythrocytes; large mononuclear cells in alveoli	Totally replaced by proliferating reticular cells occasionally arranged in foci	Many cells as in spleen; infiltrating marrow
Lungs	.....	Bronchitis, pneumonia; no essential changes	Infiltration of alveoli and alveolar walls with typical large cell	Connective tissue increased and infiltrated with single-nucleated, large, pale cells	Alveoli filled or pressed together with large, pale cells	Some capillaries with large, pigment-containing cells	Numerous mononuclear cells in alveoli	.....	Many alveoli filled with large cells
Localized mass	.....	.....	Cyst of right humerus; high-grade destruction of osseous lamellae and increased generation of tissue in cyst wall	.....	Cystic area; structure of bone totally obscured; very many large, pale cells	.....	.....	.....	Epidural mass filled with typical large, pale cells
Other findings	Infiltrations in skin of typical large cells, forming groups	.....	.....	.....	Splenic puncture; marked proliferation of reticular cells in pulp; increase in polymorphonuclears; finding suggested septicemia	.....	Cysts in each of intervertebral cartilages of lumbar vertebrae; simple loss of central substance; splenic biopsy followed by splenectomy	Infiltrations in skin of typical cells forming groups often perivascular	Splenic puncture; many red blood cells and a few pulp cells

Fig. 1.—External protrusion of the epidural mass in the left parietal region. The area over the region of the anterior fontanel is a scar which followed the removal of a nevus one year prior to the present illness.

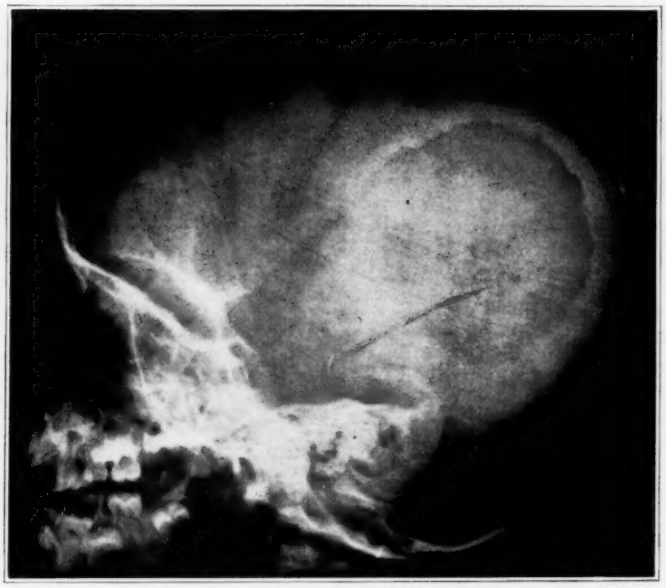

Fig. 2.—Roentgenogram (lateral view) of the skull, showing a large osseous defect.

by Guizetti and by Siwe, cystic areas were found by roentgen examination to involve the right humerus in the case of the former and the left fibula in the case of the latter. Foot-Olcott reported rarefaction of the lower part of the pelvis and of the right femur in the region of the head and osteoporosis of the spine. These lesions were discovered only by roentgen examination. In the remaining five reports, no osseous changes were noted either clinically or roentgenologically. However, with the exception of Akiba,[6] who did not include a record of the examination of the bone marrow in his report, all authors stated that in their cases there were pathologic changes in the bone marrow, which will be mentioned later.

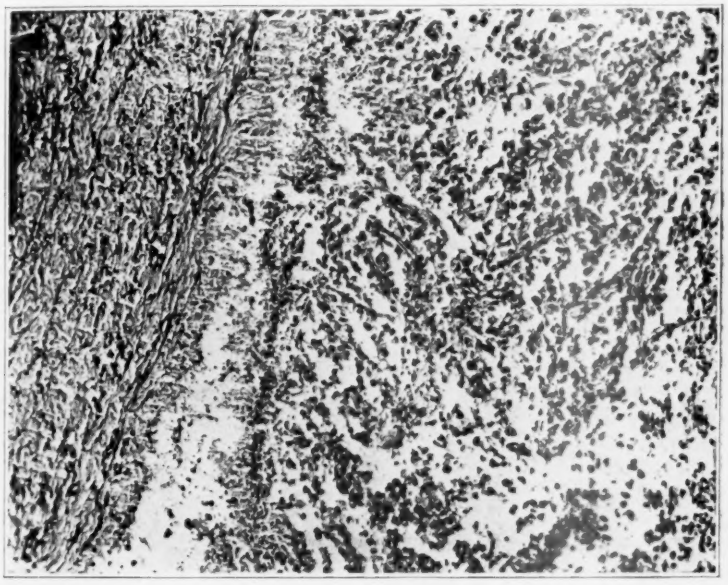

Fig. 3.—Microscopic section through the epidural mass, including the dura mater. There are many large macrophages with eccentrically situated nuclei. Hematoxylin and eosin stain; × 80.

Moderate fever was present in every instance and was of a continuous nature. There was moderate to severe secondary anemia, and the degree of anemia was commensurate with the length of the course of the disease. In our own case, anemia became progressively more severe despite several transfusions.

The highest white blood count (26,000 per cubic millimeter) was reported by Letterer. The remaining counts showed a variation from

6. Akiba, R.: Ueber Wucherung der Retikulo-Endothelien in Milz- und Lymphknoten und ihre Beziehung zu den leukämischen Erkrankungen, Virchows Arch. f. path. Anat. **260**:262, 1926.

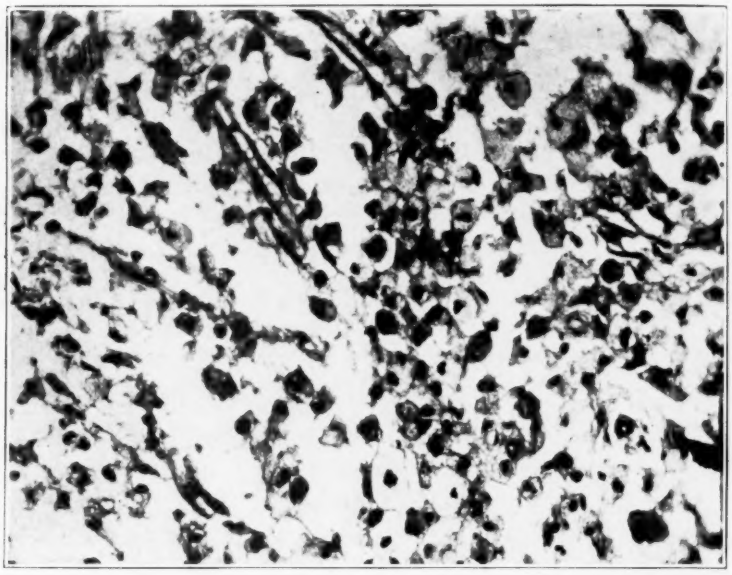

Fig. 4.—Higher magnification of typical cells in the epidural mass. Hematoxylin and eosin stain; × 325.

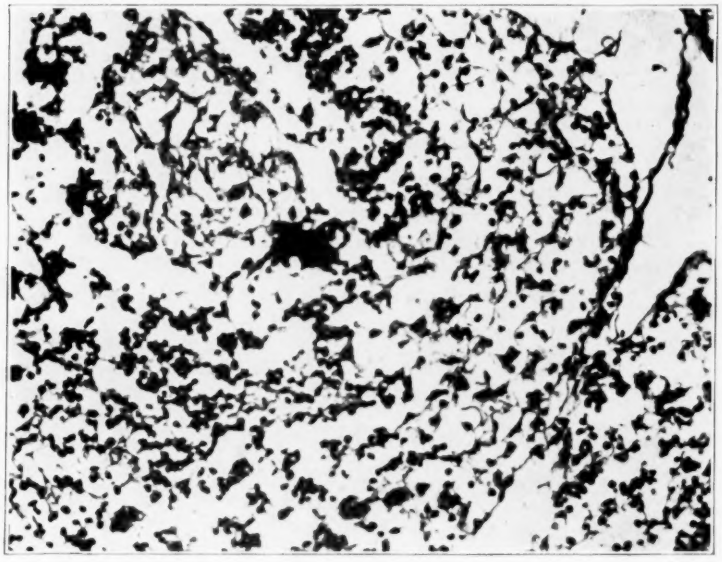

Fig. 5.—Reticulum stain from a section through the epidural mass. Foote's reticulum stain; × 325.

moderate leukocytosis to definite leukopenia, as reported by Foot and Olcott [7] and by ourselves. The differential blood count was not remarkable in any of the reported cases, save for the mononuclear cells, the proportion of which varied from 4 to 10 per cent. This we consider a slight increase above normal. The number of blood platelets varied considerably, with no persistent diminution. Blood cultures, in the three instances in which they were made, were reported to give negative results. The reaction to tuberculin injected intradermally was negative in the three patients tested, and the Wassermann reaction was negative in the instances in which the test was made. The duration of the disease was variable, the shortest reported being two weeks and the longest two years.

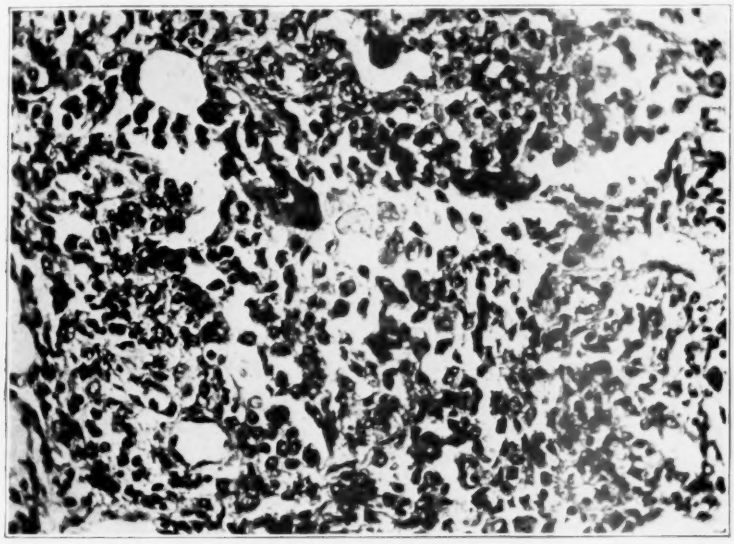

Fig. 6.—Microscopic section of a lung, showing proliferation of macrophages noted within the alveoli and in the widened alveolar septa. Hematoxylin and eosin stain; × 325.

PATHOLOGIC CHANGES

In all cases histologic sections of the liver showed diffuse fatty changes and the presence of the typical large, pale cells to a varying degree. The spleen in all studies showed structural changes, which involved a decrease to a disappearance of the lymph follicles and, in most instances, a considerable increase in the reticular fibers. Small areas of necrosis and hemorrhage were noted. In all the reported cases considerable collections of the typical large, pale nonlipoid macrophages were noted.

7. Foot, N., and Olcott, C.: Non-Lipoid Histiocytosis (Reticulo-Endotheliosis), Am. J. Path. **10**:81, 1934.

The lymph nodes showed more or less disarrangement in structure, with a proliferation of the large, pale cell in many areas supplanting the lymphatic tissue and occasionally causing small areas of necrosis.

The bone marrow is described in all the case reports except that of Akiba. The typical large, pale cells were present in foci, and there was an increase in the reticular fibers, even in those cases in which clinically and roentgenologically no bony changes could be discerned.

The lungs were not described in the reports of Letterer and Roussy and Oberling.[8] In the remaining reports it was stated that many alveoli, alveolar walls and capillaries were filled with large, pale cells. Some increase in connective tissue was also noted.

In the case described by Guizetti, a cyst of the right humerus showed high grade destruction of osseous lamellae and increased granulation tissue in the cyst wall. In the case reported by Siwe, with a cystic area in the left fibula, the bony structure was totally obscured by the infiltration of large pale cells. In the case reported by us, the bone of the skull over the left parietal area was completely eroded, and the tumor mass consisted of typical large, pale macrophages, sometimes scattered in disorganized masses but often arranged in groups about a thin, faintly outlined reticulum. Multinuclear cells were seen occasionally. Areas of necrosis were seen throughout the mass. In some regions much reddish-brown pigment was observed.

Histologic examinations of the skin were made by Letterer and Roussy and Oberling. These showed infiltrations of large, pale cells forming groups, often perivascular. In view of these observations, the cutaneous manifestations, described clinically as petechiae, may have been confused in some of the cases with the tumor-like infiltrations here described.

In the reported cases listed in table 2 it was interesting to note the variety of clinical impressions and diagnoses. A diagnosis of sepsis was made in five cases. Acute aleukemic leukemia was twice suspected. Aplastic anemia was once given as a possible diagnosis. Foot and Olcott, in order to rule out Gaucher's disease, excised a piece of spleen for biopsy and thus made a mircoscopic diagnosis of nonlipoid histiocytosis. In none of these cases was biopsy of a lymph gland performed. This procedure might prove a valuable aid for diagnosis of this condition in the future.

COMMENT

In the recent literature, a wide variety of clinically and anatomically different diseases have been associated as sub-groups under the general classification of reticulo-endotheliosis. These diseases may be grouped

8. Roussy, G., and Oberling, C.: Akute, wahrscheinlich infektiöse aleukämische Retikulose bei einem Säugling, Wien. med. Wchnschr. **84**:407, 1934.

as follows: 1. Infectious diseases, such as tuberculosis, malaria, typhoid, bacterial endocarditis and sepsis from various causes.

2. Lipoid diseases, associated with marked accumulations of various types of lipoid material, such as Gaucher's disease, Niemann-Pick's disease, Schüller-Christian's disease, xanthomatoses and diabetic lipemia.

3. Certain leukemias, in particular that termed monocytic leukemia.

4. Neoplastic diseases, such as reticulum cell sarcoma and endothelioma.

5. Lymphogranulomas, such as Hodgkin's disease.

6. Letterer-Siwe's disease, as here reported.

Similar classifications have been suggested by Epstein,[9] Chester,[10] Bock and Wiede,[11] Uehlinger [12] and Foord, Parson and Butt [13] in an attempt to correlate this variegated group into some sort of pathologic entity.

It is apparent from this classification that many unrelated diseases have been considered as so-called reticulo-endothelioses. Whenever a small or large part of the mesenchyme of the body has been found to react either in a hematopoietic or in a phagocytic direction, the condition has been termed reticulo-endotheliosis. It would seem to us that a term which is as broad and inclusive as this is of questionable aid in understanding the process involved. For a term which includes the acute pyogenic diseases, the chronic granulomatous inflammations, neoplasms and degenerative diseases with extensive lipoid storage and certain leukemias and lymphogranulomas merely signifies that quite different processes involve various parts of the connective tissue of the body.

All injuries to cells of the body call forth a connective tissue reaction. This basic reaction is irrespective of the type of stimulus. Maximow [14] stated that "the most important function of the connective tissue seems to be its active rôle in the various defense 'reactions.' . . .

9. Epstein, E.: Die generalisierten Affektionen des histiozytären Zellsystems (Histiozytomatosen), Med. Klin. **21**:1501 (Oct. 2); 1542 (Oct. 9) 1925.

10. Chester, W.: Ueber Lipoidgranulomatose, Virchows Arch. f. path. Anat. **279**:561, 1930.

11. Bock, H., and Wiede, K.: Zur Frage der leukämischen Retikuloendotheliosen (Monozytenleukämien), Virchows Arch. f. path. Anat. **276**:553, 1930.

12. Uehlinger, E.: Aleukämische Retikuloendotheliose, Beitr. z. path. Anat. u. z. allg. Path. **83**:719, 1930.

13. Foord, A. G.; Parson, L., and Butt, E. M.: Leukemic Reticulo-Endotheliosis (Monocytic Leukemia), J. A. M. A. **101**:1859 (Dec. 9) 1933.

14. Maximow, A.: Morphology of the Mesenchymal Reactions, Arch. Path. **4**:557 (Oct.) 1927.

Inflammation, whatever definition for this conception may be chosen, is by necessity always a function of the connective tissue, the medium surrounding and supporting the other elements of the body."

According to him, the following elements constitute the connective tissue:

1. Fixed, highly differentiated cells, which produce the fibrous intercellular substance in the connective tissue and plasma in the blood. These may be designated as fibrocytes. These elements are represented in the vascular system by endothelial cells and in the connective tissue by fibroblasts or fibrocytes. The same cells are present in cartilage and bone as cartilage and bone cells.

2. Fixed or free elements, which possess a marked ability for phagocytosis and vital staining. They readily resorb and store various substances, especially those of a colloidal nature. They play an important rôle in the intermediate metabolism of the body and especially in the various defense processes. . . . They may assume different characters in various parts of the body through adaptation to special local structural and functional conditions. Their fundamental properties and potencies of development are probably everywhere identical. . . . In the lymphoid and myeloid tissues and in the red pulp of the spleen, they have been known for a long time as reticular cells. In the liver they line the intralobular capillaries as the stellate cells of von Kupffer. . . . It has to be added that in the lymph nodes, the bone marrow and the spleen, the lymph sinuses and the venous sinusoids are lined by modified, flattened histiocytes, which are sometimes described as "endothelium," although they are different in their structure and behavior from true endothelium, which belongs to the group of fibrocytes. . . . (The term littoral cells has been suggested to describe these cells.)

3. Hemocytes, which are free cells, circulating in the blood and lymph and accumulating in the blood-forming organs. . . .

The cells referred to in paragraph 2 are scattered all over the body, reacting in a similar way in response to certain stimuli, and have been described under varying nomenclature. Thus, they are the macrophages of Metchnikoff,[15] the clasmatocytes of Ranvier,[16] the resting wandering cells of Maximow,[17] the adventitial cells of Marchand,[18] the rhagiocrine cells of Renault [19] and the histiocytes of Aschoff.[20]

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15. Metchnikoff, E.: Leçons sur la pathologie comparée de l'inflammation, Paris, Masson & Cie, 1892.

16. Ranvier, L.: Des clasmatocytes, Arch. d'anat. micr. **3**:123, 1900.

17. Maximow, A.: Ueber die Zellformen des lockeren Bindegewebe, Arch. f. mikr. Anat. **67**:680, 1906.

18. Marchand, F.: Ueber die bei Entzündungen in der Peritonealhöhle auftretenden Zellformen, Verhandl. d. deutsch. path. Gesellsch. **1**:63, 1898.

19. Renault, J.: Des cellules, connectives rhagocrines, Arch. d'anat. micr. **9**:495, 1907.

20. Aschoff, L.: Das reticulo-endotheliale System, Ergebn. d. inn. Med. u. Kinderh. **26**:1, 1924.

The fact that these cells respond in like manner to stimuli, particularly the elective storage of colloidal vital dyes, led to the concept that they belong to one large cell group or system, popularized by Aschoff as the reticulo-endothelial system.

We have chosen to term these cells macrophages.

With this understanding and on this basis, we shall review a few of the cases reported in the literature as examples of reticulo-endotheliosis.

Infections Termed Reticulo-Endotheliosis.—Certain diseases of known infectious etiology have been termed reticulo-endotheliosis. Coronini and Risak [21] recently pointed out that in certain types of tuberculosis of the lymph nodes not only will reticulo-endothelial hyperplasia occur in the nodes but large mononuclear cells may appear in the peripheral blood. These authors expressed the belief that owing to an infectious stimulus not only may there be a reticulo-endothelial hyperplasia throughout the lymphatic system but also certain characteristic mononuclear cells may appear in the peripheral circulation; they stated that these cells are presumably of reticulo-endothelial origin. Such a condition may closely resemble, both clinically and pathologically, other diseases characterized by a proliferation of macrophages. Yet by careful study the tuberculous nature of the condition may be established. Coronini and Risak performed a biopsy on a gland and were able to isolate tubercle bacilli, thus establishing the true diagnosis.

Acute septic infections in children may similarly call forth a response on the part of the macrophages. Krahn [22] described a case under the title "Reticuloendotheliale Reaktion oder Reticuloendotheliose," which Siwe believed was probably an instance of sepsis. Gittins [5] described four cases in a paper entitled "Anemia and Reticulo-Endotheliosis." In case 2 of his series he reported generalized staphylococcic furunculosis in a 21 month old infant, who showed at autopsy "hyperplasia of the reticulo-endothelial system with increased phagocytosis." Under the title "Ein Beitrag zu den sogenannten Reticuloendotheliosen," Uher [23] reported a case in a 20 month old infant, who following acute pneumonia suffered with a necrotizing angina. At autopsy a diffuse hyperplasia of reticulo-endothelial cells was noted in the liver, spleen, lymph nodes and lungs, and many gram-positive diplococci were seen in sections from these organs. Splenic culture revealed streptococci.

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21. Coronini, D., and Risak, E.: Zur Frage der sogenannten "akuten Retikulose," Folia haemat. **45**:171, 1931.

22. Krahn, H.: Reticuloendotheliale Reaktion oder "Reticuloendotheliose" (Leukämieform?), Deutsches Arch. f. klin. Med. **152**:179, 1926.

23. Uher, V.: Ein Beitrag zu den sogenannten Reticuloendotheliosen, Virchows Arch. f. path. Anat. **289**:504, 1933.

Sherman [24] observed generalized reticulo-endothelial hyperplasia in an 11 day old infant with erysipelas, jaundice and sepsis. A culture of the blood showed a profuse growth of streptococci.

The most recent report which we have encountered is that by Van Creveld and Ter Pooten.[25] Under the title "Infective Reticulo-Endotheliosis," they have reported a proliferation of the reticulo-endothelial system in a 4 month old child who had had otitis media since the age of 4 weeks. This infant exhibited membranous defects in the skull, and cystic foci in the humeri and ribs. The authors concluded that the condition was of an infectious etiology.

From the foregoing reports, it is clear that in definitely septic processes a generalized proliferation of the macrophages may be demonstrated. Nevertheless, the septic nature of the condition is quite obvious. It is not difficult to understand that the inflammatory process provoked a response of the connective tissue element—the macrophages.

Lipoid Storage Diseases Termed Reticulo-Endotheliosis.—The lipoid storage diseases are characterized by the accumulation of various types of lipoids. In Gaucher's disease the stored lipoid is kerasin; in Niemann-Pick's disease it is phosphatide; in Schüller-Christian's disease it is cholesterol. There is some confusion as to the nature of the processes involved, and considerable disagreement exists as to their histogenesis. Part of the confusion is obviously due to the varying interpretations of the reticulo-endothelium in the minds of various investigators.

In a recent article Pick [26] denied that Gaucher's disease is a reticulo-endothelial disease. This is probably based on Pick's thesis of the meaninglessness of the term reticulo-endotheliosis. Pick pointed out, however, that the macrophages of the liver, spleen, lymph nodes and bone marrow are involved. And, of course, these macrophages are part of the reticulo-endothelial system. The etiologic nature of Gaucher's disease is, as yet, not understood.

In 1928, Bloom [27] pointed out that in Niemann-Pick's disease there exists a lipoidemia, associated with a marked reaction on the part of the differentiated and undifferentiated mesenchyme and with what he considered secondary degenerative changes in the various epithelial, muscle,

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24. Sherman, I.: Observations on Reticulo-Endothelial Cells in Septic Jaundice, Arch. Path. **7**:78 (Jan.) 1929.

25. Van Creveld, S., and Ter Pooten, F.: Infective Reticulo-Endotheliosis, Chiefly Localized in Lungs, Bone Marrow, and Thymus, Arch. Dis. Childhood **10**: 124, 1935.

26. Pick, L.: A Classification of the Diseases of Lipoid Metabolism and Gaucher's Disease, Am. J. M. Sc. **185**:467, 1933.

27. Bloom, W.: The Histiogenesis of Essential Lipoid Histiocytosis (Niemann-Pick's Disease), Arch. Path. **6**:827 (Nov.) 1928.

ganglion and cartilage cells. Pick [28] disagreeed with this interpretation, denying that this disease is a histiocytosis, or a disease of the reticulo-endothelial system. However, as Bloom has shown, the connective tissue responds to a lipoidemia by producing more and more larger and larger macrophages, while the epithelial and other functionally specifically differentiated cells merely accumulate relatively small amounts of lipoid, which is to be regarded as a purely degenerative phenomenon. The fact that the macrophages respond to the lipoidemia in the manner described would make permissible the inclusion of Niemann-Pick's disease as one of the reticulo-endothelial diseases. For the same reason, Niemann-Pick's disease is a lipoid histiocytosis. When Pick [28] stated, "In infancy, however, as I have shown, the macrophage system is widespread, and on this account the lipoid storage takes place in many other localizations and in various organs, after the natural storage localizations are overloaded," he spoke unclearly, if, in fact, he did not err, for the macrophages are no more widespread in the infant than in the adult.

Likewise, Schüller-Christian's disease can be designated a disease of the reticulo-endothelial system, as Rowland [29] has shown that the cells involved are histiocytes. In all cases of xanthomatosis, whether the patient shows one or all of the typical manifestations, such as skeletal changes, diabetes insipidus, exophthalmos or xanthomatosis of the skin, the characteristic feature is the cholesterol-storing histiocyte. Shelling and Voshell [30] have recently reported a case in which the only changes noted were those in the skeletal system. The roentgenograms suggested osteitis fibrosa cystica, and the correct diagnosis of xanthomatosis was arrived at only after a biopsy of the bone revealed the characteristic foam cell. Schultz, Wermbter and Puhl [31] described a case under the title "Eigentümliches granulomartige Systemerkrank- und des hämatopoetischen Apparates (Hyperplasie des reticuloendothelialen Apparates)." Siwe stated the belief that this is an atypical case of Schüller-Christian's disease.

Leukemic Reticulo-Endotheliosis.—This term has been used to designate the type of leukemia reported as monocytic leukemia. Reschad and

28. Pick, L.: Niemann-Pick's Disease and Other Forms of So-Called Xanthomatosis, Am. J. M. Sc. **185**:608, 1933.

29. Rowland, R.: Xanthomatosis and the Reticulo-Endothelial System, Arch. Int. Med. **42**:611 (Nov.) 1928.

30. Shelling, D., and Voshell, A.: Xanthomatosis Generalisata Ossium, Arch. Int. Med. **55**:592 (April) 1935.

31. Schultz, Wermbter and Puhl: Eigentümliche granulomartige System erkrankung des hämatopoetischen Apparates (Hyperplasie des reticuloendothelialen Apparates), Virchows Arch. f. path. Anat. **252**:519, 1924.

Schilling-Torgau [32] were the first to note a case of such leukemia, in which the monocytes seemed to be the predominating cell in the circulating blood. In the past few years, reports of cases of monocytic leukemia have become more and more frequent. Clough,[33] in 1932, was able to collect tweny-three such cases. Recent reports by Doan and Wiseman,[34] Foord, Parsons and Butt [13] and Forkner [35] have added to the increasing number of the cases reported.

The interest in monocytic leukemia lies in the speculation, first, as to whether this is a true third type of leukemia and, second, as to the origin of the monocytic cells found in the peripheral blood. Neither question has been answered with any degree of proof or experimental fact. In many of the cases in which a predominance of circulating monocytes was observed during life the condition has at autopsy proved to be myelosis. Gittins and Hawksley [36] have recently reported such an instance in a 10 month old infant.

Naegeli [37] expressed the belief that a distinct monocytic type of leukemia does not occur and that this type passes into myeloid leukemia if the patient lives long enough. The diagnosis of monocytic leukemia has rested on the clinical finding of a predominant number of monocytic cells in the peripheral blood and on the pathologic demonstration that the tissues show an extensive leukemic infiltration with monocytic cells. It has been assumed that the cells seen in the blood-forming tissues at autopsy enter the circulation as monocytes, but there is no definite evidence of such an occurrence. Clough stated that clinically monocytic leukemia resembles acute leukemia of other types; Forkner, on the other hand, stated the belief that severe ulcerative and necrotic gingivitis is characteristic of monocytic leukemia. In our opinion, this would be a rather difficult clinical differentiation. Mononuclear erythrophagocytosis has been reported in cases of monocytic leukemia.[38]

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32. Reschad and Schilling-Torgau: Ueber eine neue Leukämie, München. med. Wchnschr. **60**:1981, 1913.

33. Clough, P.: Monocytic Leukemia, Bull. Johns Hopkins Hosp. **51**:148, 1932.

34. Doan, C., and Wiseman, B.: The Monocyte, Monocytosis, and Monocytic Leukosis, Ann. Int. Med. **8**:383, 1934.

35. Forkner, C.: Clinical and Pathologic Differentiation of Acute Leukemias with Special Reference to Acute Monocytic Leukemia, Arch. Int. Med. **53**:1 (Jan.) 1934.

36. Gittins, R., and Hawksley, J.: Monocytic Reaction in Myelosis, Arch. Dis. Childhood **8**:241, 1933.

37. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, ed. 5, Berlin, Julius Springer, 1931.

38. Abt, Arthur F.: Mononuclear Erythrophagocytosis in the Blood of a New-Born Infant, Am. J. Dis. Child. **42**:1364 (Dec.) 1931.

The origin of the monocytic cells noted in the peripheral blood in the cases of leukemia under discussion is the second speculative problem which has interested all the observers reporting these cases. Each writer has had his own theory and has speculated accordingly. Maximow and Bloom [39] summarized the main theories of the origin of the monocytes as follows: (1) endothelium; (2) myeloblasts; (3) macrophages, and (4) lymphocytes.

The claim that the monocytes originate from the fixed macrophages (or from histiocytes, or from the reticulo-endothelial system) in different parts of the body is the link which binds monocytic leukemia to the so-called reticulo-endothelioses. Most of the current writers favor this origin of the circulating monocytes and of the monocytic cells seen on pathologic section. If it could be proved that these monocytes originate from the fixed macrophages, then monocytic leukemia would be proved to be a disease of the reticulo-endothelial system, and it would also be proved to be a third and distinct type of leukemia.

This theory of the origin of the monocytes from the fixed macrophages assumes an entirely independent origin for the myeloid, lymphocytic and monocytic cell; it is known as the trialistic theory of hematopoiesis. It is further assumed that the fixed macrophages mobilize and give rise to small cells that enter the circulating blood and have, for the most part, lost their capacity for storing vital dyes. The possibility of the origin of the monocytes from the reticulo-endothelial system must be admitted, according to Maximow, but it has never been experimentally proved.

Klostermeyer [40] has recently reported an interesting case under the title "Ueber eine sogenannte aleukämische Reticulose mit besonderer Beteilung des Magen-Darmkanales." Clinically, the points of chief interest were swelling of the face, nodules over the scalp, splenohepatomegaly, marked leukopenia (2,000 cells per cubic millimeter) with 99 per cent lymphocytes, many of which were pathologic types, and marked generalized lymphadenopathy. Pathologically, the gross examination revealed an involvement of the entire lymphatic system, which was unusually marked in the gastro-intestinal tract. Histologically, however, there was a hyperplasia of reticulo-endothelial cells combined with an increase in reticular fibers in various organs. Although the histologic picture was dominated by the hyperplasia of macrophages, the clinical symptoms, the blood findings and the gross involvement of the entire

39. Maximow, A., and Bloom, W.: A Text-Book of Histology, ed 2, Philadelphia, W. B. Saunders Company, 1934.

40. Klostermeyer, W.: Ueber eine sogenannte aleukämische Reticulose mit besonderer Beteilung des Magen-Darmkanales, Beitr. z. path. Anat. u. z. allg. Path. **93**:1, 1934.

lymphatic system would lead one to assume that one was dealing with an acute lymphatic leukemia, associated with reticulo-endothelial hyperplasia. This is probably an example of acute lymphatic leukemia in which the reticulo-endothelial system showed a marked hyperplasia.

Tumors Involving Reticulo-Endothelium.—While, on the one hand, the noninvasive hyperplasia of leukemia bears a resemblance to the hyperplasias which, according to Schultz,[41] may be the result of infection, inflammation or toxemia, on the other hand, the chloroma group of leukemias, usually with local tumor formation, may exhibit varying degrees of invasiveness of a neoplastic character.

Gittins and Hawksley[42] have reported a case in which leukemia, tumor and reticulo-endothelial hyperplasia were combined. Bilateral endotheliomas of the ovaries were observed in a 1 year old child. Following extirpation of these tumors, a monocytic type of leukemia developed. At autopsy, the various organs were infiltrated with monocytic cells, similar to those noted in the peripheral blood, and there was a hyperplasia of reticulo-endothelial cells. This case illustrates the association of tumor and leukemia, with hyperplasia of the macrophages.

Roulet[43] has reported on a series of tumors of the lymph glands in which the sarcomatous cellular findings have been associated with varying degrees of hyperplasia of reticular fibers. Roulet termed these tumors "primary lymph gland retothelsarcoma."

We have pointed out that connective tissue responds to various abnormal stimuli, and it is therefore not surprising to find an increase in reticular fibers in neoplastic involvement of lymph glands. No one has proved whether the part played by the reticulo-endothelial cells in these tumors is of a primary or of a secondary nature. However, the involvement of reticulo-endothelium in certain neoplasms forces one to include tumors under the general heading of reticulo-endotheliosis.

Hodgkin's Disease (Lymphogranulomatosis), Termed Aleukemic Reticulosis.—Recently in reports on Hodgkin's disease emphasis has been placed on the proliferation of reticular cells and the increase in the reticular fibers.[44] Certain authors have seen fit to include Hodgkin's disease among the reticulo-endothelioses and would term it aleukemic reticulosis. Hodgkin's disease presents a fairly typical clinical picture.

41. Schultz, O., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1926, vol. 8, p. 838.

42. Gittins, R., and Hawksley, J.: Reticulo-Endotheliomatosis, Ovarian Endothelioma, and Monocytic (Histiocytic) Leukemia, J. Path. & Bact. **36**:115, 1933.

43. Roulet, F.: Das primäre Retothelsarkom der Lymphknoten, Virchows Arch. f. path. Anat. **277**:15, 1930.

44. Dameshek, W.: Aleukemic Reticulosis, Folia haemat. **49**:64, 1933.

The etiology of the condition is unknown. Edith Potter [45] recently pointed out that histologically the only specific feature of Hodgkin's disease is the Hodgkin cell. Other histologic findings, such as loss of structure, invasion of the capsule of the lymph node, hyperplasia of the reticulum cells and increase in the number of eosinophils, are not specific for Hodgkin's disease and may occur in other diseases of the lymph nodes. However, even without a definite knowledge of the etiology, the characteristic clinical picture associated with the histologic appearance of the typical Hodgkin cell would still enable one to establish the diagnosis of this condition and name it Hodgkin's disease. We agree that the proliferation of the macrophages entitles this disease to a place among the reticulo-endothelioses. However, naming it aleukemic reticulosis does not aid in the diagnosis, treatment or prognosis of the condition, and we believe that the change of name simply confuses the time-honored place and standing which this disease has always had.

Letterer-Siwe's Disease.—The case which we have reported has clinical and pathologic features similar to the one first described by Letterer in 1924 and to those collected by Siwe in 1933. The clinical picture is characterized by splenohepatomegaly, generalized lymphadenopathy, hemorrhagic cutaneous manifestations, anemia and osseous changes occurring in infancy. In these cases, no definite etiology could be ascertained. Pathologically, there is a widespread hyperplasia of the macrophages, without lipoid storage, in the various organs. These cases, as Siwe has shown, can definitely be separated from those having a somewhat similar clinical picture, but in which a hyperplasia of the macrophages occurs as an expression of various infections, lipoid storage diseases, leukemias, neoplastic diseases and Hodgkin's disease. In view of these facts, it would seem plausible to group these cases as instances of a clinical pathologic entity, under the term Letterer-Siwe's disease.

For the reasons given in this discussion on the classification of the so-called reticulo-endothelial diseases, we do not feel justified in appending the term reticulo-endotheliosis to the title. We have attempted to emphasize the all inclusiveness and meaninglessness of the term reticulo-endotheliosis. While we agree that the condition which we have described may be included under this term, we do not believe that its use would aid in clarifying the understanding of the disease.

CONCLUSIONS

We have reported a disease, occurring in an infant, which was characterized clinically by splenohepatomegaly, generalized lymphadenopathy, hemorrhagic cutaneous manifestations, anemia and osseous changes. Pathologically, there was a widespread hyperplasia of nonlipoid-storing

45. Potter, E.: Hodgkin's Disease, Arch. Path. **19**:139 (Feb.) 1935.

macrophages in the liver, spleen, lymph glands, bone marrow and lungs. The etiology of this disease is unknown.

The literature was reviewed, and it was found that eight similar cases have been reported. The first instance of this condition was cited by Letterer, in 1924, and Siwe, in 1933, was the first to collect and group these cases. We have, therefore, proposed the term Letterer-Siwe's disease as appropriate for this condition.

A discussion of the so-called reticulo-endothelial diseases has been presented. It has been emphasized that under the term reticulo-endotheliosis a wide variety of diseases, some of known and others of unknown etiology, have been grouped. We have attempted to point out that there is no advantage, either for clinical diagnosis or for pathologic classification, in grouping these heterogeneous conditions under the term reticulo-endotheliosis.

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CHANGES IN LUNG VOLUME DURING TREATMENT WITH ARTIFICIAL PNEUMOTHORAX FOR LOBAR PNEUMONIA

REPORT OF THREE CASES

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The effect of artificial pneumothorax on vital capacity has been studied by various observers, including Bendove,[1] Anthony and Heine,[2] Schill,[3] Sieper [4] and Kochs,[5] by the usual methods of spirometry. However, reports of complete studies of the volume of the lungs are extremely rare, since the determination of the residual air (or the subtidal volume) depends on indirect measurements by some gas dilution and rebreathing technic. We are familiar with only one study on artificial pneumothorax in which such complete data are given (Anthony and Heine [6]). This work deals with the effects of artificial pneumothorax in collapse therapy for pulmonary tuberculosis. In their study, readings of intrapleural pressure are not recorded, nor are roentgen studies complete. Determination of residual air was made by a hydrogen dilution method.

The employment of artificial pneumothorax in the treatment of lobar pneumonia in children at this hospital in an attempt to estimate its

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1. Bendove, R. A.: Vital Capacity in Artificial Pneumothorax, Arch. Int. Med. **36**:94 (July) 1925.

2. Anthony and Heine: Spirographische Untersuchungen bei Lungenkollaps, Beitr. z. Klin. d. Tuberk. **71**:362, 1929.

3. Schill, E.: Pneumothoraxstudien; über den Zusammenhang von Vitalcapacität, Pneumothoraxdruck und Lungenkollaps bei mit Pneumothorax behandelten Lungenkranken, Beitr. z. Klin. d. Tuberk. **65**:492, 1927.

4. Sieper, H.: Die Vitalkapazität bei der Lungenphthise, besonders bei der Lungenkollapstherapie, Beitr. z. Klin. d. Tuberk. **65**:725, 1927.

5. Kochs, K.: Studien über die Vitalkapazität bei künstlichen Pneumothorax, Beitr. z. Klin. d. Tuberk. **73**:734, 1930.

6. Anthony, A. J., and Heine: Spirographische Untersuchungen bei Lungenkollaps, Beitr. z. Klin. d. Tuberk. **73**:51, 1929.

clinical efficacy has given us the opportunity to observe the volume of the lungs in its component parts in a group of three cases, which are included in another paper.[7] The results obtained seem to be significant from several standpoints: by demonstrating the effects of lobar pneumonia itself on the volume of the lungs; by measuring the effect of known amounts of air introduced under manometric control on the various components of the volume of the lungs, and more especially by demonstrating the effect of considerably positive intrapleural pressure obtained in therapeusis in the cases to be reported.

DEFINITIONS

For the purpose of clarity in the presentation of our material, we shall define the components of the total volume of the lungs as we employ them. An excellent discussion of this subject is found in Christie's paper.[8] The definitions are as follows:

Subtidal Volume (functional residual): The air content of the lung at the conclusion of a normal tidal expiration.

Vital Capacity: The volume of air expired during a forced expiratory effort after the deepest possible inspiration.

Complemental Air: The volume of air inspired from the level of normal inspiration to the maximal inspiratory level.

Supplemental Air: The volume of air expired from the level of normal expiration (resting expiratory level) to the maximal expiratory level.

Mean Tidal Air: The average volume of air inspired or expired between the normal inspiratory and expiratory levels.

Total Volume: The air content of the lung at the maximal inspiratory level (that is, the sum of complementary, mean tidal and subtidal air).

METHODS

The determinations of lung volume were made always with the patient in a supine horizontal position. The head was supported by one or two small pillows. This constant position obviated any changes in volume owing to change in body posture.[9] Conditions of fasting were not ordinarily observed. In the acutely pneumonic stage diet was not of significance, but care was taken not to make a determination within two hours after a meal during convalescence.

The determination of the subtidal volume by the technic to be described is independent of any voluntary effort on the part of the subject. Determinations of

7. Harper, P.: Treatment of Lobar Pneumonia in Children by Artificial Pneumothorax, Am. J. Dis. Child., this issue, p. 536.

8. Christie, R. V.: The Lung Volume and Its Subdivisions: I. Methods of Measurement, J. Clin. Investigation **11**:1099 (Nov.) 1932.

9. Hurtado, A., and Fray, W.: Studies of Total Pulmonary Capacity and Its Subdivisions: III. Changes with Body Posture, J. Clin. Investigation **12**:825 (Sept.) 1933.

vital capacity, on the contrary, depend on a considerable degree of cooperation, more so than one can expect in the average acutely ill child. Therefore, we have limited the study to three especially suitable cases in older and very cooperative patients.

The determinations of the subtidal volume of the lungs were made according to the oxygen dilution, rebreathing technic described by Christie [8] in 1932. This method has been used successfully in the study of the normal and the emphysematous patient by Hurtado and others [10] and in the study of the mechanism of postoperative pulmonary complications by Beecher.[11] The details of the method may be obtained in the original article. It will suffice here to state that the method depends on the mixing of the alveolar nitrogen in the subject's lungs with air in the closed circuit of a spirometer of known dead space (in this instance, 1,260 cc.). To the spirometer is added a controlled volume of oxygen, which sustains the metabolism during the course of the determination (from five to seven minutes), the unutilized portion effecting a dilution of the nitrogen in the lung-spirometer system. A gasometric analysis for the nitrogen percentage of the sample of mixed gas in the spirometer after the period of rebreathing is concluded makes it possible to calculate the subtidal pulmonary volume.

The vital capacity and its component parts were measured as follows: The patient was connected by an ordinary rubber mouthpiece, with lips and nose sealed, to the Roth-Benedict recording spirometer used in the Christie method. The spirometer was filled with a mixture of air and oxygen, approximately 50 per cent. The patient was allowed to breathe quietly for ten or twelve respirations and then caused to inspire as deeply as possible and then expire forcibly. At intervals of from fifteen to thirty seconds this maneuver was repeated until stable maximal values were recorded on the spirometer record. The values for complemental and supplemental air were all computed from the curves for vital capacity thus recorded.

RESULTS

The results are here expressed by the reproduction of the protocols of the three cases.

CASE 1 (case 16 in the previous paper [7]).—C. K., a Negro girl aged 13, weighing 76 pounds (34.5 Kg.) and 55 inches tall (139.7 cm.), was well until April 18, 1935, when she contracted a cold in the head. On April 20 there were some fever and cough and pain in the left side. On April 21 the child seemed better and went for a walk in the morning, but in the afternoon she had malaise with three shaking chills. On the morning of April 22 she was admitted to the New Haven Hospital.

Her temperature was 104.5 F., her pulse rate 130 and her respiratory rate 52. She appeared acutely ill, with rapid respirations, dilatation of the alae nasi and occasional respiratory grunts. There were hyperesthesia and splinting of the lower portion of the chest on the left side; the percussion note was impaired over the

10. Hurtado and Fray.[9] Hurtado, A., and Boller, C.: Studies of Total Pulmonary Capacity and Its Subdivisions: I. Normal Absolute and Relative Values, J. Clin. Investigation **12**:793, 1933. Hurtado, A.; Kaltreider, N. L.; Fray, W. W.: Brooks, W., and McCann, W. S.: Studies of Total Pulmonary Capacity and Its Subdivisions: VI. Observations on Cases of Obstructive Pulmonary Emphysema, ibid. **13**:1027 (Nov.) 1934.

11. Beecher, H. K.: Effect of Laparotomy on Lung Volume: Demonstration of a New Type of Pulmonary Collapse, J. Clin. Investigation **12**:651 (July) 1933.

lower lobe of the left lung, and over the same area the breath sounds were suppressed and a few fine râles were heard. A roentgen examination of the chest at 11 a. m. failed to reveal conclusive signs of pulmonary consolidation. There was a slight haziness in the lower lobes of both lungs, more marked on the left side and in the perihilar area of the lower lobe of the left lung. Studies of lung volume were made between 5 and 6 p. m. The patient was quite ill and not very cooperative, so it was possible to obtain only the subtidal and the mean tidal volume, which were 990 and 270 cc., respectively. Roentgen examination at 7 p. m. revealed a diffuse haziness throughout the midportion of the left lung, extending from the hilus to the lateral wall of the chest. The process was well visualized in the lateral view and had the appearance of a pneumonic infiltration in the upper half of the lower lobe of the left lung (fig. 1 *A*).

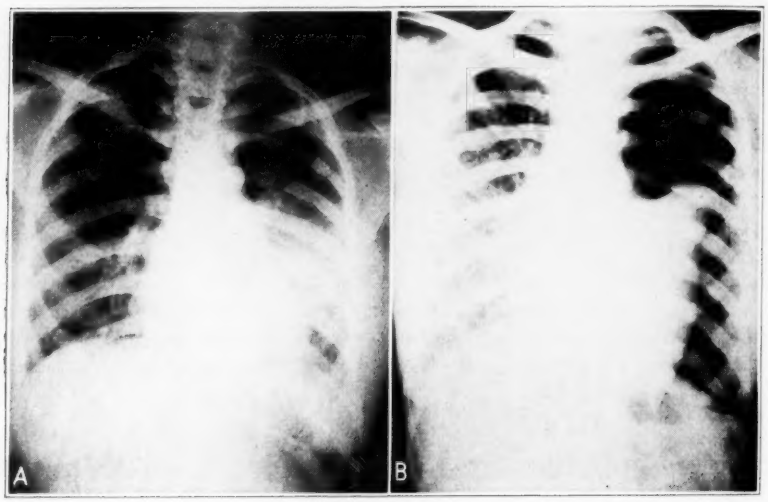

Fig. 1 (case 1).—*A*, roentgenogram of the chest taken at 7 p. m. on April 22, 1935; *B*, maximal collapse after completion of injections of air on April 24, 1935.

At 8:20 p. m. on April 22 a thoracentesis was performed on the left side. The initial pressures were —5 and —3 cm. of water. Eight hundred and fifty cubic centimeters of air was slowly introduced into the left side of the thoracic cavity, following which the intrapleural pressure was +3 on inspiration and +7 on expiration. At 4 a. m. on April 23, 200 cc. of air was introduced, and at 8 a. m., 100 cc. Following the last injection the value for intrapleural pressure on inspiration was +4 and on expiration +8. Studies of lung volume were carried out at 2 p. m. with the following results: subtidal volume, 800 cc.; vital capacity, 520 cc.; supplementary air, 60 cc.; mean tidal air, 220 cc.; complementary air, 240 cc.; total volume, 1,260 cc. At this time a roentgen examination of the chest showed collapse of the entire left lung, which occupied approximately one fourth of the hemithoracic volume. The trachea and heart were markedly shifted to the right, and the left dome of the diaphragm was depressed. The intercostal spaces were widened. There was no demonstrable free fluid, and the right lung remained clear.

TABLE 1 (case 1).—*Data on Therapy with Artificial Pneumothorax in a Patient with Lobar Pneumonia*

			Pneumothorax Data					Lung Volume, Cc.						
			Initial Pressure		Final Pressure		Air Injected, Cc.	Subtidal Volume	Vital Capacity	Supplementary Air	Mean Tidal Air	Complementary Air	Total	Comment and Roentgen Findings
Date	Hour	Procedure	Insp.	Exp.	Insp.	Exp.								
4/22/35	5:00 p.m.	Lung volume....						990			270			
	8:20 p.m.	Thoracentesis....	−5	−3	+3	+7	850							
4/23/35	4:00 a.m.	Thoracentesis....	+1	+5	+4	+8	200							
	8:00 a.m.	Thoracentesis....	+3	+6	+4	+8	100							
	2:00 p.m.	Lung volume....						800	520	60	220	240	1,260	Left lung collapsed ¼ hemithoracic volume
4/24/35	9:25 a.m.	Thoracentesis....	+1	+5	+4	+7	250							
	11:00 a.m.	Lung volume....						760	480	60	220	200	1,180	Left lung occupies ⅓ hemithoracic volume
4/29/35	11:00 a.m.	Lung volume....						840	940	160	180	600	1,620	Lung collapsed as before
	4:00 p.m.	Thoracentesis....	−2	+2	−7	−4	−500							Air withdrawn
4/30/35	2:00 p.m.	Thoracentesis....	−6	−4			−200							Air withdrawn
	2:50 p.m.	Lung volume....						1,110	1,280	250	240	790	2,140	
5/ 3/35	2:00 p.m.	Lung volume.....						1,240	1,440	360	280	800	2,320	Reexpansion nearly complete; thin film of air remains
5/11/35	12:00 m.	Lung volume....						1,250	1,440	320	360	760	2,370	Complete reexpansion

On April 24 at 9:25 a. m. a fourth thoracentesis was performed. The initial pressures were +1 and +5. Following the injection of 250 cc. of air the pressures were +4 and +7. The lung volume was determined at about 11 a. m., with the following results: subtidal volume, 760 cc.; vital capacity, 480 cc.; supplementary air, 60 cc.; mean tidal air, 220 cc.; complementary air, 200 cc.; total volume, 1,180 cc. A roentgenogram taken of the patient in a prone position revealed collapse of the left lung. It appeared to fill approximately from one fourth to one fifth of the left side of the thorax. There was a moderate displacement of the mediastinum toward the right. Fluid was not visualized in this film. A roentgenogram taken with the patient in an erect position showed a small fluid level in the inferior portion of the left side of the thorax and the left costophrenic sinus. The collapse of the left lung in this position appeared to be more marked, and a definite adherence of a portion of the upper part of the collapsed lung was noted in the region of the third rib anteriorly. The mediastinal shift was not so marked in this position (fig. 1 *B*). No further injections of air were made.

On April 29, 1935, determinations of lung volume were made at 11 a. m. and the following values obtained: subtidal volume, 840 cc.; vital capacity, 940 cc.; supplementary air, 160 cc.; mean tidal air, 180 cc.; complementary air, 600 cc.; total volume, 1,620 cc. More roentgenograms taken of the chest revealed the left lung still collapsed to about the same degree as at the previous examination. A very small amount of fluid was noted in the left costophrenic sinus. At 4 p. m. a thoracentesis was performed. The initial pressures were —2 and +2. Five hundred cubic centimeters of air was withdrawn, with resulting intrapleural pressures of —7 and —4. On the following day at 2 p. m. an additional 200 cc. of air was withdrawn. The initial pressures were —6 and —4. Determinations of lung volume were carried out at 2:50 p. m., and the following values were obtained: subtidal, 1,110 cc.; vital capacity, 1,280 cc.; supplementary, 250 cc.; mean tidal, 240 cc.; complementary, 790 cc.; total volume, 2,140 cc.

On May 3, 1935, another roentgen examination of the chest showed good reexpansion of the left lung. There was only a small amount of pneumothorax, noted chiefly in the left apical region. The lungs were well aerated throughout. The trachea and heart were in normal position. On this date, a determination of lung volume was carried out at 2 p. m. The results were: subtidal, 1,240 cc.; vital capacity, 1,440 cc.; supplementary, 360 cc.; mean tidal, 280 cc.; complementary, 800 cc.; total volume, 2,320 cc.

The patient's temperature fell by steady lysis and was normal ninety-six hours after the first pneumothorax was performed. She was discharged from the hospital on May 4. On May 11 a final series of determinations of lung volume was made. The patient was ambulatory at that time and feeling well. The lungs were clear on physical examination, and roentgenograms showed complete reexpansion, with no residual fluid or consolidation. The results of determinations of lung volume were: subtidal volume, 1,250 cc.; vital capacity, 1,440 cc.; supplementary air, 320 cc.; mean tidal air, 360 cc.; complementary air, 760 cc.; total volume, 2,370 cc.

CASE 2 (case 14 of the previous paper [7]).—J. M., a white boy aged 14½ years, weighing 131 pounds (59.4 Kg.) and 70 inches tall (177.8 cm.), had pneumonia during 1927. Two days before admission to the hospital he went to bed about noon because of headache. During the afternoon, he had a cough and fever, and rusty sputum appeared in the evening. On the day before admission his temperature was 102 F. He was seen by a physician, who diagnosed the condition as bronchitis and probably pneumonia. On March 19, with the cough and fever persisting, he was

TABLE 2 (case 2).—*Data on Therapy with Artificial Pneumothorax in a Patient with Lobar Pneumonia*

			Pneumothorax Data					Lung Volume, Cc.						
			Initial Pressure		Final Pressure		Air Injected, Cc.	Subtidal Volume	Vital Capacity	Supplementary Air	Mean Tidal Air	Complementary Air	Total	Comment and Roentgen Findings
Date	Hour	Procedure	Insp.	Exp.	Insp.	Exp.								
3/19/35	3:30 p.m.	Lung volume....						1,510	1,540	280	360	900	2,770	
	5:10 p.m.	Thoracentesis....	—7	—4	0	+3	1,050							
	7:10 p.m.	Lung volume.....						1,090	1,220	200	300	720	2,110	
	10:25 p.m.	Thoracentesis....	—1	+1	+1	+5	700							
3/20/35	3:25 a.m.	Thoracentseis....	—1	+4	+1	+7	350							Following this injection the right lung appeared collapsed one half
	1:20 p.m.	Thoracentesis....	0	+4	+4	+7	600							
	7:50 p.m.	Thoracentesis....	0	+4	+3	+7	500							
3/21/35	9:20 a.m.	Thoracentesis....	+2	+4	+5	+9	140							
3/22/35	9:10 a.m.	Thoracentesis....	+3	+5	+3	+7	200							
3/27/35	3:30 p.m.	Lung volume....						950	1,200	180	340	680	1,970	
3/29/35		Thoracentesis....	—4	0	—6	—2	—700							Air removed
4/ 1/35		Thoracentesis....	—6	—4	—8	—6	—600							Air removed
4/ 4/35	10:30 a.m.	Lung volume....						1,590	1,870	360	410	1,100	3,100	
4/11/35		Lung volume.....						1,830	2,720	490	610	1,620	4,060	Good expansion

admitted to the New Haven Hospital. The temperature on admission was 104 F., the pulse rate 122 and the respiratory rate 36. Significant physical findings were confined to the chest, which presented signs of consolidation in the right lower lobe.

A stereoroentgenographic examination of the chest showed an abnormal density involving the lower portion of the right lung. The density was sharply demarcated at its upper border and did not extend into the costophrenic sinus. A roentgenogram of a lateral view of the chest revealed a collection of fluid in the interlobar fissure between the middle and the lower lobes of the right lung. In the lower posterior portion of the lung was a dense area which had the appearance of a pneumonic process. The rest of the lung was clear; findings in the heart and mediastinum were not remarkable (fig. 2 *A*). Determinations of lung volume were made beginning at 3:30 p. m., with the following results: subtidal volume, 1,510 cc.; vital capacity, 1,540 cc.; supplementary air, 280 cc.; mean tidal air, 360 cc.; complementary air, 900 cc.; total volume, 2,770 cc. Artificial pneumo-

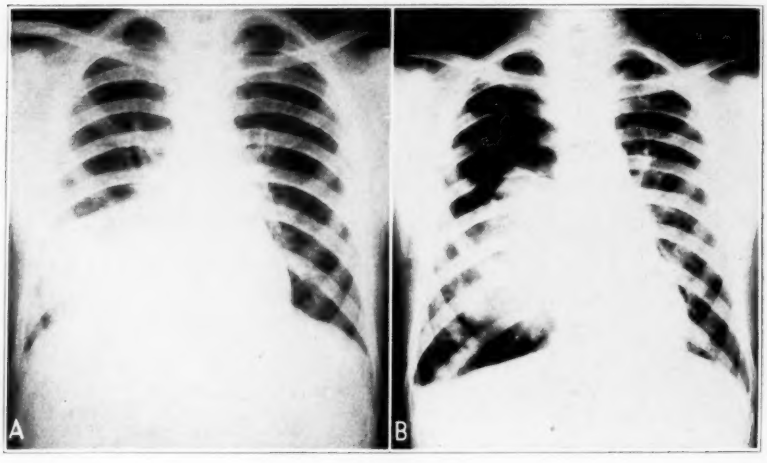

Fig. 2 (case 2).—*A*, roentgenogram of the chest taken at the time of admission on March 19, 1935; *B*, roentgenogram taken on March 25, 1935.

thorax on the right side was begun at 5:10 p. m. The initial pressures were —7 and —4 cm. of water. After the injection of 1,050 cc. of air, the final pressures, at 6:55 p. m., were 0 and +3.

Studies of lung volume were repeated at 7:10 p. m., with the following results: subtidal volume, 1,090 cc.; vital capacity, 1,220 cc.; supplementary air, 200 cc.; mean tidal air, 300 cc.; complementary air, 720 cc.; total volume, 2,110 cc. At 10:25 p. m. the intrapleural pressures were —1 and +1. After the injection of 500 cc. of additional air, the final readings were +1 and +5. On March 20 at 3:25 a. m. the intrapleural pressures were —1 and +4. Subsequent to the injection of 350 cc. of air the final pressures were +1 and +7.

Another roentgen examination of the chest following these three injections of air (totaling 1,900 cc.) showed on the right side a partial collapse of all lobes, occupying approximately one half of the hemithoracic volume. In the posteroanterior projection a portion of the lung extended to the right lateral thoracic cage, and in the lateral projection, to the posterior wall, suggesting adhesions between the

visceral and the parietal layer of the pleura. There was some fluid in the lateral and posterior portions of the costophrenic sinus. There was a slight shift of the trachea and heart to the left; the left lung remained clear.

On the same day at 1:20 p. m. the pressures were 0 and +4. Following the injection of 600 cc. of air, they rose to +4 and +7. At 7:50 p. m. they were 0 and +4. Following the injection of 500 cc. of air, the pressures were +3 and +7. On March 21, 1935, the initial pressures at 9:20 a. m. were +2 and +4, and following the injection of 140 cc. of air, +5 and +9. On March 22 at 9:10 a. m. the readings were +3 and +5; following the injection of 200 cc. of air, +3 and +7. No further injections of air were made. The patient's temperature fell by crisis seventy-two hours after the first treatment with artificial pneumothorax.

On March 25, 1935, roentgen examination of the chest with the patient in an erect position revealed a hydropneumothorax on the right side. A portion of the right lung was apparently held to the lateral wall of the chest in the lower half of the right side of the thorax. In this region there were several air-containing spaces with fluid levels in their inferior portions. They were all of small size, the largest being about 2 cm. in diameter. The heart was displaced somewhat to the left, and the markings of the left lung were accentuated (fig. 2 *B*).

On March 27, 1935, beginning at 3:30 p. m., the following values for lung volume were obtained: subtidal volume, 950 cc.; vital capacity, 1,200 cc.; supplementary air, 180 cc.; mean tidal air, 340 cc.; complementary air, 680 cc.; total volume, 1,970 cc.

On March 29, 1935, a tap made on the left side of the chest revealed initial pressures of —4 and 0. Following the removal of 700 cc. of air, the pressures were —6 and —2. On April 1, 1935, the initial pressures were —6 and —4. Following the removal of 600 cc. of air they were —8 and —6.

Determinations of lung volume were repeated on April 4, 1935, with the following results: subtidal volume, 1,590 cc.; vital capacity, 1,870 cc.; supplementary air, 360 cc.; mean tidal air, 410 cc.; complementary air, 1,100 cc.; total volume, 3,100 cc.

The patient's course was clinically satisfactory, and he was discharged from the hospital on April 4. He returned to the hospital on April 11 for roentgen examination and determinations of lung volume. Roentgen examination at this time revealed a very thin film of air surrounding the entire right lung. The air was scarcely discernible and most noticeable in the upper part of the chest on the right side. The possibility of some of this appearance being due to thickened pleura was considered. The right pulmonary field was slightly hazy as compared with the left, but no definite infiltration was present. Determinations of lung volume at this time gave the following results: subtidal volume, 1,830 cc.; vital capacity, 2,720 cc.; supplementary air, 490 cc.; mean tidal air, 610 cc.; complementary air, 1,620 cc.; total volume, 4,060 cc.

CASE 3 (case 13 in the previous paper [7]).—S. G., a white boy aged 14, weighing 99 pounds (44.9 Kg.) and 62½ inches tall (158.8 cm.), fell ill on March 12, 1935, approximately at noon, with a chill, followed by fever and prostration. He spent a restless night. The following morning pain developed in the left side on deep breathing, and a cough was noted. On March 14 he was admitted to the New Haven Hospital with a temperature of 105.8 F., a pulse rate of 114 and a respiratory rate of 28. The physical signs were those of beginning consolidation in the lower lobe of the left lung.

TABLE 3 (case 3).—*Data on Therapy with Artificial Pneumothorax in a Patient with Lobar Pneumonia*

Date	Hour	Procedure	Pneumothorax Data: Initial Pressure Insp.	Initial Pressure Exp.	Final Pressure Insp.	Final Pressure Exp.	Air Injected, Cc.	Lung Volume, Cc.: Subtidal Volume	Vital Capacity	Supplementary Air	Mean Tidal Air	Complementary Air	Total	Comment and Roentgen Findings
3/14/35	2:15 p.m.	Lung volume....						1,700	2,030	400	380	1,250	3,330	
	3:05 p.m.	Thoracentesis....	−7	−5.5	−1	+2	750							Subsequent roentgenogram showed partial collapse and fluid in costophrenic sinus
	4:30 p.m.	Lung volume....						1,150	1,320	180	400	740	2,290	
	8:05 p.m.	Thoracentesis....	−2	0	+2	+6	600							
	11:45 p.m.	Thoracentesis....	0	+4	+3	+8	200							
3/15/35	11:00 a.m.	Thoracentesis....	+2	+5	+3	+7	150							
	4:00 p.m.	Thoracentesis....	+2	+6	+3	+7	150							Lung collapsed to ¼ of hemothoracic volume
	10:30 p.m.	Thoracentesis....	0	+4	+3	+7	300							
3/16/35	10:50 a.m.	Lung volume.....						1,050	840	80	300	460	1,810	
	11:00 a.m.	Thoracentesis....	+2	+7	+4	+8	125							
	11:40 a.m.	Lung volume.....						960	750	80	320	350	1,630	
	10:40 p.m.	Thoracentesis....			+3	+7	100							
3/19/35	7:25 p.m.	Thoracentesis....	+3	+7	−1	+2	−450							Air removal
3/20/35	3:20 p.m.	Lung volume....						810	600	100	280	220	1,310	Rapid accumulation of fluid
6/14/35	3:00 p.m.	Lung volume....						1,980	2,580	470	560	1,550	4,090	Reexpansion complete except for 10 cc. sinus tract

Roentgen examination of the chest at the time of admission revealed a pneumonic process involving the lower portion of the lower lobe of the left lung only. There was no evidence of pleural effusion. At 2:15 p. m. on the day of admission determinations of lung volume were made, and the following values were obtained: subtidal volume, 1,700 cc.; vital capacity, 2,030 cc.; supplementary air, 400 cc.; mean tidal air, 380 cc.; complementary air, 1,250 cc.; total volume, 3,330 cc. Thoracentesis on the left side was performed at 3:05 p. m. The initial pressures were —7 and —5.5. Seven hundred and fifty cubic centimeters of air was injected, following which the pressures rose to —1 and +2, respectively. Roentgen reexamination of the chest revealed a partial collapse of the left lung with a small amount of effusion noted in the left costophrenic sinus. There was no evidence of a selective collapse.

Determinations of lung volume at 4:30 p. m. revealed the following values: subtidal volume, 1,150 cc.; vital capacity, 1,320 cc.; supplementary air, 180 cc.; mean tidal air, 400 cc.; complementary air, 740 cc.; total volume, 2,290 cc.

Further injection of air was begun at 8:05 p. m. The initial pressures were —2 and 0. Subsequent to the injection of 600 cc. of air, the pressures were +2 and +6. At 11:45 p. m. an additional 200 cc. of air was introduced, with final pressure readings of +3 and +8.

Roentgen examination of the chest on the morning of March 15 showed a collapse of the entire left lung, which occupied approximately one fourth of the hemithoracic volume. There was some tenting of the apex and the extreme lower portion of the left lung, possibly due to adhesive bands. There was no evidence of effusion, and the right pulmonary field was clear. During the day, the patient received 600 cc. of air in three doses, and the final pressure readings were +3 and +7 at 10:30 p. m.

On March 16, 1935 at 10:50 a. m. readings for lung volume were as follows: subtidal volume, 1,050 cc.; vital capacity, 840 cc.; supplementary air, 80 cc.; mean tidal air, 300 cc.; complementary air, 460 cc.; total volume, 1,810 cc. Thoracentesis was performed at 11 a. m.; the initial pressures were +2 and +7. One hundred and twenty-five cubic centimeters of air was injected, with resulting pressures of +4 and +8. Determinations of lung volume were repeated after the injection at 11:40, with the following values obtained: subtidal volume, 960 cc.; vital capacity, 750 cc.; supplementary air, 80 cc.; mean tidal air, 320 cc.; complementary air, 350 cc.; total volume, 1,630 cc.

At 10:40 p. m. on March 16 an additional 100 cc. of air was injected, with final pressure readings of +3 and +7. Roentgen reexamination on March 17 revealed the left lung collapsed to approximately one-fourth its usual size. The mediastinum was pushed to the right, without evidence of herniation. There was a small amount of fluid in the left costophrenic sinus (fig. 3 *A*). On March 19, 1935, at 7:25 p. m. the initial pressures were +3 and +7. Following the removal of 450 cc. of air the pressure dropped to —1 and +2. On March 20 determinations of lung volume were made at 3:20 p. m., with the following results: subtidal volume, 810 cc.; vital capacity, 600 cc.; supplementary air, 100 cc.; mean tidal air, 280 cc.; complementary air, 220 cc.; total volume, 1,310 cc. A roentgen reexamination of the chest the same afternoon showed a rather prominent shift of the trachea and heart to the right. The costophrenic sinus on the left was entirely obliterated, and a horizontal fluid level occupied the lower portion of the left side of the chest, extending to the level of the eighth rib in the midaxillary line; the right lung remained clear (fig. 3 *B*).

Aspiration of the fluid from the left side of the chest revealed a thin, purulent material, which on culture yielded Pneumococcus type I and Bacillus influenzae.

The patient's chest was then tapped repeatedly until March 30, when an open thoracotomy was carried out with resection of a portion of the seventh rib for drainage of the pyopneumothorax. The patient showed a slow but steady clinical improvement thereafter. Roentgen examination on April 27 showed some residual collapse of the left lung, but definite expansion was noted, and no fluid level was present. On June 10, the residual cavity contained 30 cc. of air, and roentgen examination on June 12 revealed complete reexpansion of the left lung except for a small pocket at the site of the drainage. There was some thickening of the pleura on this side. The cavity held from 10 to 15 cc. on June 13. There was never any evidence of a bronchopleural fistula.

On June 14 final determinations of lung volume were made with the following results: subtidal volume, 1,980 cc.; vital capacity, 2,580 cc.; supplementary air, 470 cc.; mean tidal air, 560 cc.; complementary air, 1,550 cc.; total volume, 4,090 cc.

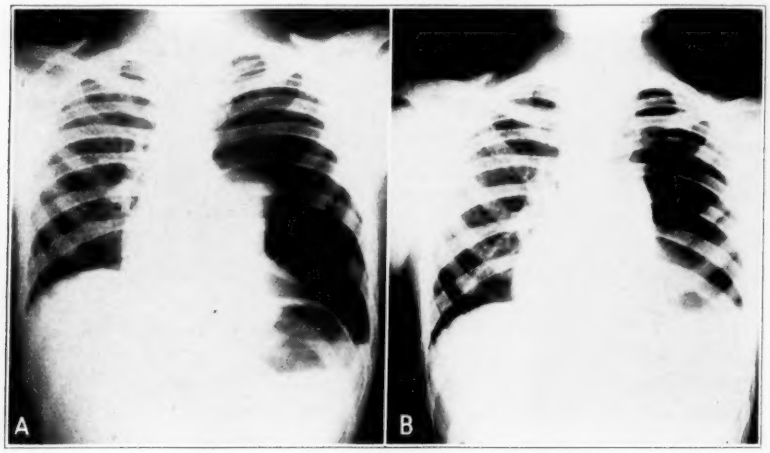

Fig. 3 (case 3).—*A*, roentgenogram taken on March 17, 1935, at the height of the pneumothorax collapse; *B*, roentgenogram taken on March 20, 1935, showing the large accumulation of fluid.

COMMENT ON RESULTS

A comparison of the initial determinations of the subtidal volume of the lungs and the final values recorded during the convalescence indicates that the subtidal volume is considerably reduced during the early stages of lobar pneumonia. In case 1, although the initial roentgenogram showed little evidence of infiltration, the reduction in subtidal volume was 20 per cent. There was also a significant reduction in the mean tidal exchange, this being in association with an accelerated respiratory rate. Binger and Brow [12] reported in 1924 the result of determinations of the volume of residual air for ten patients with penumonia by their hydrogen

12. Binger, C. A. L., and Brow, G. R.: Studies on Respiratory Mechanism in Lobar Pneumonia: Study of Lung Volume in Relation to Clinical Course of Disease, J. Exper. Med. **39**:677 (May) 1924.

dilution technic. They concluded that the residual volume followed closely the clinical progress of the disease.

The introduction of measured amounts of air into one pleural space was followed by a decrease in the subtidal volume of the lungs, but less quantitatively than the volume of air introduced. Likewise the withdrawal of air in measured quantities from an existing pneumothorax caused a rise in the subtidal volume, but less than the amount of air withdrawn. Numerous factors contribute to the discrepancies. When large volumes of air are introduced into the pleural cavity, there is an increase in the size of the chest, which can be demonstrated in these cases physically and by roentgen measurements. There is also a drop in the level of the diaphragm toward the inspiratory position. Shifts in the mediastinum and pleural adhesions may be complicating factors. A redistribution of the volume of blood in the pulmonary fields and the large venous reservoirs of the mediastinum must likewise be considered. One may, however, conclude that the physiologic adjustments following the introduction of large volumes of air into the thorax act in a direction to preserve a subtidal (functional residual) volume sufficient to the needs of the patient at the expense of the complemental air, which is drastically reduced.

SUMMARY

Complete studies of lung volume by the technic of Christie have been carried out in three cases of lobar pneumonia during treatment with artificial pneumothorax.

Lobar pneumonia was associated with a reduction in the subtidal volume of the lungs early in the disease, as compared with the values during convalescence.

The introduction of measured quantities of air into one pleural cavity was attended by decreases in the subtidal volume of the lungs, but always quantitatively less than the volume of introduced air. Similarly, the withdrawal of air from a pneumothorax cavity caused a rise in the subtidal volume, but less than the amount of air removed.

A gradual reduction in the subtidal volume to a level only 50 or 60 per cent of the normal was not attended by a failure of the mechanism of external respiration, even in the presence of infection in the respiratory tract.

TREATMENT OF LOBAR PNEUMONIA IN CHILDREN BY ARTIFICIAL PNEUMOTHORAX

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This communication reports a study of the treatment of lobar pneumonia with artificial pneumothorax in twenty-two children, without fatality. It is obvious that any such clinical study is difficult to evaluate and that no final conclusions can be drawn from relatively few cases.

The literature on this form of therapy in children under 16 years of age is summarized in table 1. Only forty of the fifty-one cases reported in the literature may be classified as instances of lobar pneumonia, and among these were several in which the condition was of long duration and was complicated by interlobar effusions (Ibrahim and Duken,[1] and Jahr and Neuman[2]). The patients with bronchopneumonia showed pathologic changes that were chiefly unilateral. Certain differences between the condition in the group reported in the literature and that in our cases are noteworthy. Only 31 per cent of the patients in the former group were treated on or before the fourth day of illness, while my group includes no patient seen after the fourth day. Furthermore, my patients in whom pneumothorax was instituted received air in larger volumes and at shorter intervals. In pursuing this course I adopted the plan of Blake, Howard and Hull,[3] who, as a result of their experience with pneumothorax in adults with lobar pneumonia, thought that success depended on early and fairly complete collapse of the entire lung of the involved side.

In planning the study many difficulties were anticipated. Some children were too young to give voluntary cooperation; the dangers associated with the mobile mediastinum of children and with possible herniation of the mediastinum were not underestimated. I had no information as to the amount of air to be given, the frequency or number of treatments or the optimum changes in interpleural pressure to be attained for patients in any of the age groups.

This investigation was aided by a grant from the Research Fund, Yale University School of Medicine.

From the Department of Pediatrics, Yale University School of Medicine and the Pediatric Service of the New Haven Hospital and Dispensary.

1. Ibrahim, J., and Duken, S.: Zur Behandlung der kindlichen Pneumonie mit dem künstlichen Pneumothorax, Arch. f. Kinderh. **84**:241 (July 20) 1928.

2. Jahr, J., and Neuman, R.: Zur Pneumothorax-Behandlung der Säuglingspneumonie, Klin. Wchnschr. **9**:2200 (Nov. 22) 1930.

3. Blake, F. G.; Howard, M. E., and Hull, W. S.: The Treatment of Lobar Pneumonia by Artificial Pneumothorax, Tr. A. Am. Physicians **49**:119, 1934.

TABLE 1.—*Cases of Pneumonia in Children Treated with Artificial Pneumothorax Reported in the Literature*

Year	Author	Age Range	Cases by Day of Disease That First Injection of Air Was Done									Amount of Air at First Treatment, Cc.	Interval, Hours	Amount of Air at Second Treatment, Cc.	Total Treatments		Recovery	Fatal	Empyema	Classification of Pneumonia	
			2	3	4	5	6	7–14	15+	Not Given	Total				Number	Cc. of Air				Lobar	Bronchial
1921	David: Deutsche med. Wchnschr. **47**: 802, 1921	8 wk. to 3 yr.	..	..	1	1	..	2	..	..	4	?	?	?	?	?	4	0	0	4	..
1929	Klotz: Monatschr. f. Kinderh. **42**: 312, 1929	5 to 9 yr.	..	..	1	..	1	..	1	1	4	170-500	24-240	?-300*	1-3	500-600*	3	1	0	1	3
1928 and 1930	Ibrahim and Duken [1]																				
1930	Duken: Klin. Wchnschr. **9**: 2195, 1930	8 wk. to 3 yr.	..	..	..	..	..	4	3	..	7	100-250+	18-48	75-400	1-8	525-1,600*	7	0	0	7	..
1930	Jahr and Neuman [2]	6 wk. to 6 mo.	..	1	1	1	..	2	..	..	5	?	?	?	?	?	4	1	0	5	..
1931	Popowski and Stankiewiez: Rev. franç de pédiat. **7**: 619, 1931	6 mo. to 11 yr.	..	..	..	..	..	2	5	3	10	40-300	24-72	80-300	1-3	220-640	9	1	0	3†	7
1932	Coghlan: Lancet **1**: 13, 1932	9 yr.	..	..	1	..	..	..	..	..	1	150	72	100	2	250	1	0	0	1	..
1932	Li: Chinese M. J. **46**: 886, 1932	8 yr.	..	..	..	..	..	..	..	1	1	170	24	80	3	370	1	0	0	1	..
1934	Moorman: Internat. Clin. **4**: 118, 1934	2 to 15 yr.	..	1	1	..	..	2	..	..	4	180-400	12-18	125-200	1-2	205-600	4	0	1	3	1
1934	Behrend and Cowper: J. A. M. A. **102**: 1907 (June 9) 1934	15 yr.	..	..	..	1	..	..	..	..	1	400	18	500	2	900	1	0	0	1	..
1934	Crowell: South. Med. & Surg. **96**: 467, 1934	1 to 9 yr.	..	..	1	1	..	..	..	1	3	75-180	14-18	90-200	2-4	165-680	3	0	0	3	..
1934	Blake, Howard and Hull [3]	13 yr.	..	..	1	..	..	..	..	..	1	.....	.....	.....	...	.....	1	0	0	1	..
1935	Holmes and Randolph: Ann. Int. Med. **8**: 1008, 1935	.....	..	1	6	1	..	2	..	..	10	125-300	18-48	100-300	1-4	175-1,250	8	2	4	10	..
	Totals.....	.....	0	3	13	5	1	14	9	6	51	40-500	12-72	75-500	1-8	165-1,250	46	5	5	40	11
	Harper	15 mo. to 15 yr.	4	16	2	..	..	..	..	..	22	100-1,050	4-10‡	50-600	2-10	275-3,350	22	0	3	22	

* Complete data were not given.
† Three cases were classified by the authors as instances of gangrène pulmonaire profonde.
‡ This does not include the case of bilateral pneumonia in which only two treatments were given, seventy-two hours apart.

MATERIAL AND PLAN OF STUDY

Pneumothorax therapy was used for all patients with recognized unilateral lobar pneumonia admitted to the pediatric service of the New Haven Hospital within seventy-two hours after onset between Oct. 1, 1934, and April 15, 1935. Subsequently, one other patient was selected for treatment because of adaptability to measurements of the volume of the lungs. In addition, I treated one patient with bilateral lobar pneumonia of four days' duration whose history and physical and roentgen findings suggested an early contralateral spread; air was injected into the recently affected side. The youngest patient was 15 months of age, and the oldest was 15 years. Fourteen were male, and eight were female.

Serial postero-anterior and lateral roentgenograms were made. A patient was not treated until there was distinct roentgenographic as well as physical evidence of consolidation, this requirement sometimes causing a delay of twelve or more hours. Observations were recorded of the changes in interpleural pressure (inspiratory, expiratory and mean), the amount and speed of injections of air, the leukocyte response, the titer of humoral antibodies and the results of cultures of the blood. Serial studies of lung volume were carried out on three patients, the values being correlated with roentgenograms and readings of interpleural pressure.[4]

Bacteriologic diagnoses were made by the conventional method of intraperitoneal inoculation of white mice with swabbings from the nose and throat and subsequent typing by the Sabin method.[5] The time of appearance and the titer of humoral antibodies were determined by mouse protection tests. Two-tenths cubic centimeter of the patient's serum was injected intraperitoneally into white mice coincidentally with 0.5 cc. of tenfold dilutions of an eight hour broth culture of a homologous pneumococcus. The pneumococcus used was of such virulence that 1×10^{-7} cc. (0.0000001 cc.) of the culture was invariably fatal; protection tests were made with 1, 10, 100 and 1,000 minimal lethal doses.

As the work progressed, changes were gradually made in the plan and method of treatment. Data will be presented to trace this development.

PLAN OF TREATMENT

Preliminary Medication.—It was first necessary to select a drug for sedative or anesthetic purposes. Tri-bromethanol was used for the first nine patients in doses of from 50 to 100 mg. per kilogram of body weight. The drug gave fairly satisfactory results in most patients, the anesthetic action usually lasting from one to two hours, and there was no depression of the respiration or other untoward reaction. The drug did, however, have certain disadvantages. The initial operation for pneumothorax was sometimes delayed in children who objected to and expelled the rectal instillation. In the few cases in which the anesthetic effect was not adequate for the entire period of injection of air, the patient became difficult to handle as the anesthesia became light. The administration of fluids was a serious problem in some patients, the natural difficulties of giving adequate liquid to febrile children being aggravated by the repeated administration of tri-bromethanol.

Codeine sulfate gave good results in one child of 8 years.

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4. Lindskog, G.; Harper, P., and Friedman, I.: Changes in Lung Volume During Treatment with Artificial Pneumothorax for Lobar Pneumonia: Report of Three Cases, this issue, p. 523.

5. Sabin, A. B.: The Microscopic Agglutination Test in Pneumonia, J. Infect. Dis. **46**:469 (June) 1930.

Morphine sulfate, avoided in the early period of the study because of fear of its depressing effect, was used for the last twelve patients and was most satisfactory. In the usual dosage it gave an excellent sedative effect in ten of the twelve children. Fear of a strange procedure was lost, and remarkable cooperation was obtained, with many children sleeping in naps during the injection of air. Fluids were given without interruption. In two children more than the usual dose, as calculated by Young's rule, was required.

Position of the Patient.—The first patient was placed in the lateral recumbent position, with the involved side uppermost and the pneumothorax needle inserted just below the angle of the scapula. On the third treatment with the patient in this position 500 cc. of air was given, the mean interpleural pressure coming to 0. When the patient was turned on his back at the end of the procedure he at once complained of difficulty in breathing and a sense of oppression over the chest. Dyspnea appeared, and a few râles were heard over the uninvolved lung. Two hundred and fifty cubic centimeters of air was at once withdrawn, the symptoms being relieved by the time half of this amount had been removed. It was then noted that the change from the lateral recumbent to the supine position caused an increase in the mean intrapleural pressure, which in this patient amounted to 7 cm. of water. Thus, the mean interpleural pressure of 0 with the patient in the lateral recumbent position was increased to a mean pressure of 7 cm. of water by turning him flat on his back. Similar readings in the two positions were subsequently made on twelve children. In two there was no change in the interpleural pressure with the change in position. In the other ten the change from the lateral to the supine position resulted in an increase in interpleural pressure of from 1 to 7 cm. of water, the average increase being about 4 cm. It was also observed that pressure on the abdomen either manually or by placing the patient prone caused an even more marked increase in the interpleural pressure, suggesting that this position should be avoided. Further investigation is needed to determine the relation between these findings and the amount of air injected, the presence of adhesions and the mobility of the mediastinum. Since it was not possible in an individual case to prognosticate what the increase in pressure would be and because the patients were in a supine position during most of the febrile period, it was decided to carry out all future injections of air with the patient on his back, with the needle inserted in the third or fourth interspace between the midaxillary and the anterior axillary lines. It must be remembered, therefore, that readings of the interpleural pressure were from 0 to + 7 cm. of water higher than they would have been if our patients had been treated in the lateral recumbent position.

Speed of Injection of Air and Interpleural Pressure.—The speed of injection, the amount of air to be injected and the level to which the interpleural pressure was raised underwent progressive modification, always tending toward a slower rate of injection of a larger amount of air in an effort to obtain earlier and more complete collapse. Observations on six representative cases are given in the figures to show changes made in the plan of treatment as experience developed. Cases 2 and 5 represent failure of pneumothorax therapy, resulting, in my opinion, from the early method of injecting relatively small amounts of air at infrequent intervals. The air was introduced at a rate of from 10 to 12 cc. a minute; the mean interpleural pressure was never raised above + 2 cm. of water and frequently fell to negative levels. The data for case 2 are presented in figures 1 and 2. The child was the second patient and was considered an unusually favorable subject for pneumothorax, thoracentesis being carried out at a time, forty-eight hours

after onset, when the roentgenogram showed an early pneumonic infiltration in the upper lobe of the right lung. After two injections of air totaling only 425 cc., roentgen examination revealed the right lung to be more than half collapsed, with no evidence of adhesions. Instead of increasing this early collapse, an inadequate amount of air (50 cc.) was given during the next thirty-six hours, and the lung reexpanded and formed adhesions at the level of the second rib in the axillary line.

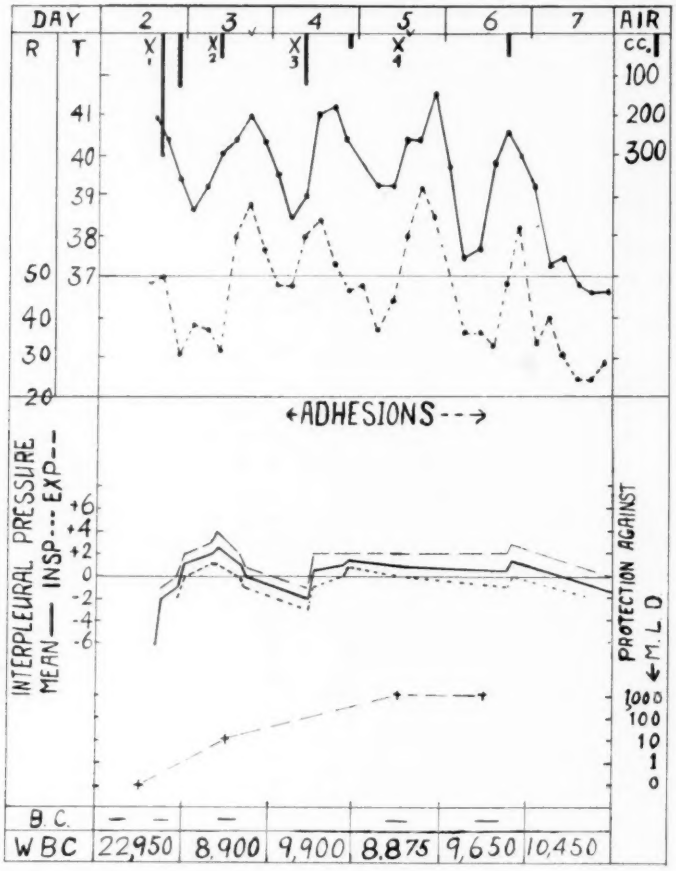

Fig. 1 (case 2).—A child, 7 years old, had pneumonia, with involvement of the upper lobe of the right lung. Pneumococcus type I and H. influenzae were recovered.

The adhesions prevented collapse; the patient continued to be actively ill for five days and then had a crisis. The handling of adhesions will be discussed later.

The data for case 5 are presented in figures 3 and 4. The roentgenogram (fig. 4, *1*) made on the patient's admission to the hospital shows consolidation of the entire upper lobe of the right lung. Only small amounts of air were injected, and during the important first twenty-four hours of treatment the interpleural pressure was not increased above 0. Although a critical fall in temperature

occurred within thirty-six hours there were two recurrences of fever, which, as can be seen in figure 3, were coincident with a fall in the interpleural pressure.

The record for case 11 (figs. 5 and 6) shows an early modification of the technic. While the amount of air given at each thoracentesis was only slightly increased, injections of air were given at shorter intervals and were more numerous, so that the total amount of air given was greater and the mean interpleural pressure was carried to higher positive levels, especially during the early hours of treatment by compression. As shown in figure 6, the film made before treatment showed early infiltration in the upper lobe of the right lung, and fairly good compression was obtained in spite of a small adhesion.

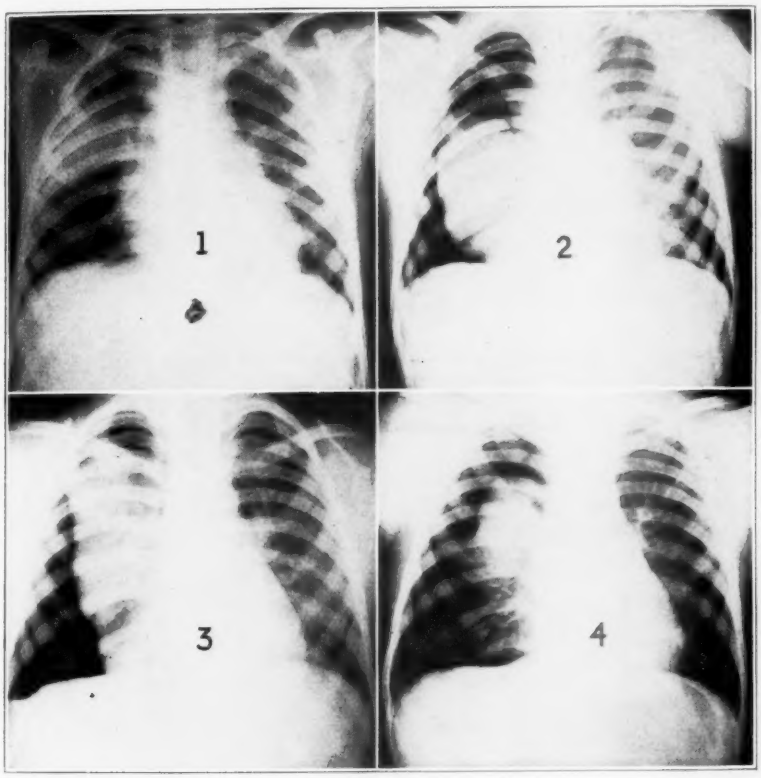

Fig. 2 (case 2).—Serial roentgenograms, showing: *1*, the condition before treatment; *2*, sixteen hours later, after the injection of 425 cc. of air, with no evidence of adhesions on original roentgenogram, although they may be suggested in the reproduction; *3*, twenty-four hours later, after the lung has reexpanded and is attached to the lateral thoracic wall at the level of the second rib, and *4*, after five days, with separation of the adhesions and partial collapse of the pneumonic upper lobe, while the uninvolved lower lobes are beginning to reexpand.

The present technic, although still susceptible of improvement, is illustrated by cases 1, 20 and 21. The amount of the initial injection of air was greatly increased,

and the spread of injection was decreased, from 7 to 9 cc. of air being given each minute. By injecting air thus slowly, higher levels of interpleural pressure and more extensive collapse could be obtained during the first twenty-four hours, with little or no discomfort for the patient. In each of the three patients the mean interpleural pressure reached + 6 cm. of water within twelve hours after beginning therapy. Satisfactory levels of pressure for different age groups will be suggested later. Fewer injections were given, and it is suggested that the air given

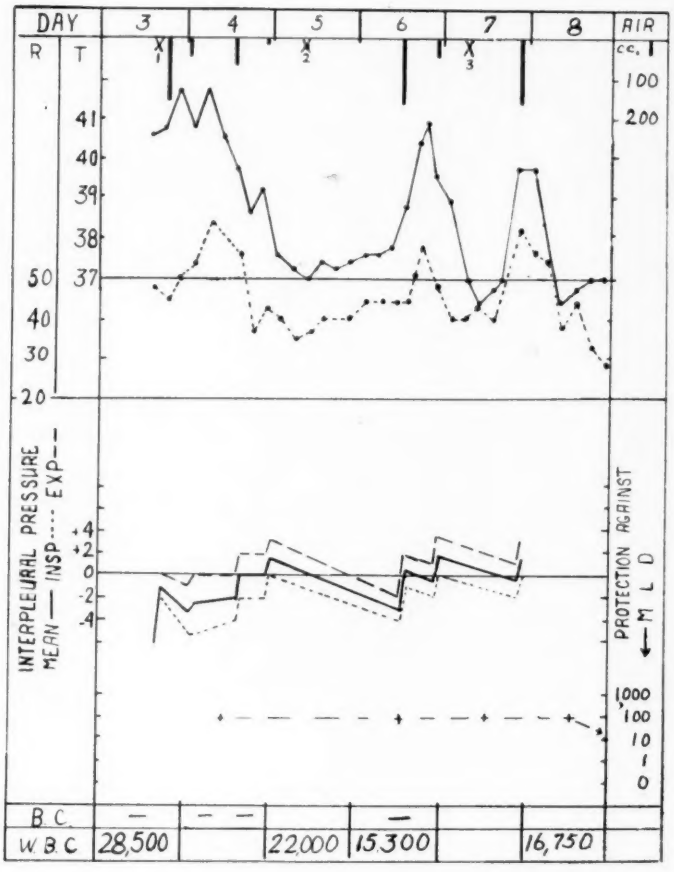

Fig. 3 (case 5).—A boy, 4 years old, had pneumonia, with involvement of the upper lobe of the right lung. Pneumococcus type I and H. influenzae were recovered.

on the third injection in cases 20 and 21 might well have been divided between the second and the fourth injection.

The patient in case 1 (figs. 7 and 8) was the only one to be treated in the lateral recumbent position, and it was only in retrospect, after making corrections for this difference in position, that I realized that the procedure used for this first patient was much like the latest technic, in that the interpleural pressure was early carried to high levels.

The charts and roentgenograms (figs. 9 to 12) for cases 20 and 21 are self-explanatory. Case 21 illustrates one of the difficulties in evaluating the results of pneumothorax therapy. The critical fall in temperature, which occurred sixteen hours after the initiation of pneumothorax, was followed by a secondary rise of temperature to a peak of 38.6 C. (99.6 F.), and the right eardrum was observed to have ruptured spontaneously and to be draining profusely twenty-four hours after the onset of this secondary rise.

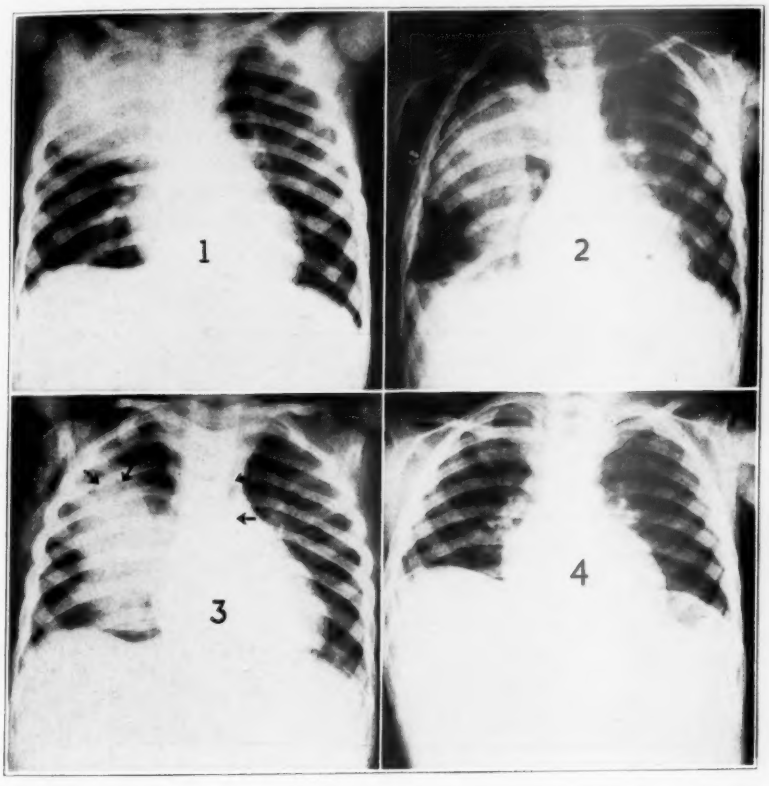

Fig. 4 (case 5).—Serial roentgenograms, showing: *1*, the condition before treatment, with diffuse infiltration of the upper lobe of the right lung; *2*, poor collapse forty-two hours later after only 300 cc. of air was injected; *3*, collapse still poor after five more days (the arrows on the left point to the edge of the mediastinal hernia), and *4*, reexpansion fourteen days after the onset.

Reexpansion.—It was thought that reexpansion should be well advanced before the patient was discharged. In several children this process was aided by a withdrawal of air at intervals of one or two days. The removal of air was best carried out in smaller amounts and at no faster rate than the speed at which air had been injected. Otherwise severe and distressing episodes of coughing ensued. That reexpansion could be greatly accelerated by careful removal of air is shown by

the roentgenograms for case 20 (fig. 10). Most of the children were discharged with slight residual pneumothorax and were to return for check-up at intervals of one or two weeks. All patients showed complete reexpansion within two weeks of the time of discharge except the patient in case 12, whose sterile effusion is commented on later, and one other patient, who did not return for check-up.

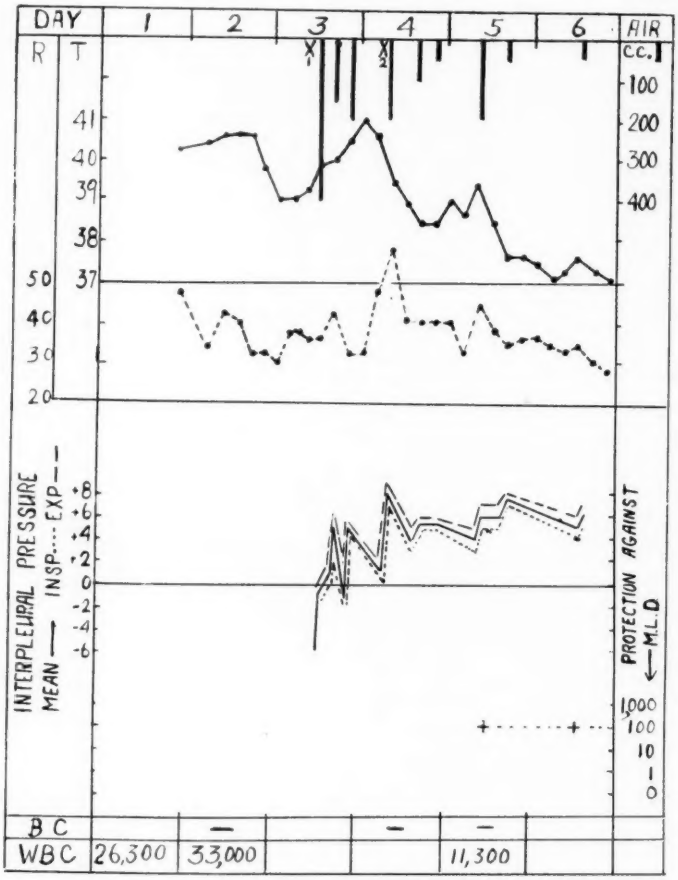

Fig. 5 (case 11).—A boy, 5 years old, had pneumonia, with involvement of the upper lobe of the right lung. Pneumococcus type I was recovered.

EVALUATION OF DATA

For the evaluation of the data first the seven cases in which there was complication by preexisting fibrous adhesions or empyema will be considered and then the cases of fifteen children in whom some benefit should have been expected if the therapy was of value.

Table 2 gives the data for the three patients with empyema and the four with preexisting fibrous adhesions. All the patients in this group

TABLE 2.—*Cases with Empyema or Preexisting Fibrous Adhesions*

Case	Age, Years	Bacteria*	Blood Culture	Site		First Treatment			Second Treatment		All Later Treatment			Total Treatments		Result	Recovery	
				Lung	Lobe	Day	Hours after Onset	Air, Ce.	Intervals, Hours	Air, Ce.	Number	Intervals, Hours	Air, Ce.	Number	Air, Ce.		Hours after First Treatment	Day of Disease
3	6	P. I	++	L	L	3	52	300	8	125	1	17	25	3	450	Empyema; recovery	...	..
9	7	P. I	—	R	U	3	54	350	10	375	3	10-36	475	5	1,200	Empyema; recovery	...	..
13	14	P. I and H. inf.	—	L	L	3	53	750	4	600	6	4-12	1,075	8	2,425	Empyema; recovery	...	..
14	14	P. I	—	R	L	3	48	1,050	5	500	5	5-24	1,800	7	3,350	Crisis	72	6
22	13	P. XIV	—	L	L	3	54	850	6	200	2	4-25	350	4	1,400	Lysis	96	6
7	1, 11 mo.	P. I and P. XVIII	—	R	U	3	53	200	6	50	2	10	275	4	525	Lysis	108	7
12	15	P. I	+	R R R L	U† M L L	3	54	750	4	500	2	6-8	500	4	1,750	Lysis	108	8

* In this and the following tables P. means pneumococcus and H. inf., Haemophilus influenzae.

† Progressive spread of pneumonic process from R. U. to R. M., to R. L., to L. L.

were first treated on the third calendar day of the disease. Pneumococcus type I was recovered from both the throats and the pleural exudate of the patients with empyema, and Haemophilus influenzae was recovered from both sources from one child. As soon as the presence of empyema was established the injection of air was stopped, and air was removed from the pleural cavity in amounts sufficient to prevent undue rise in interpleural pressure as the amount of empyema

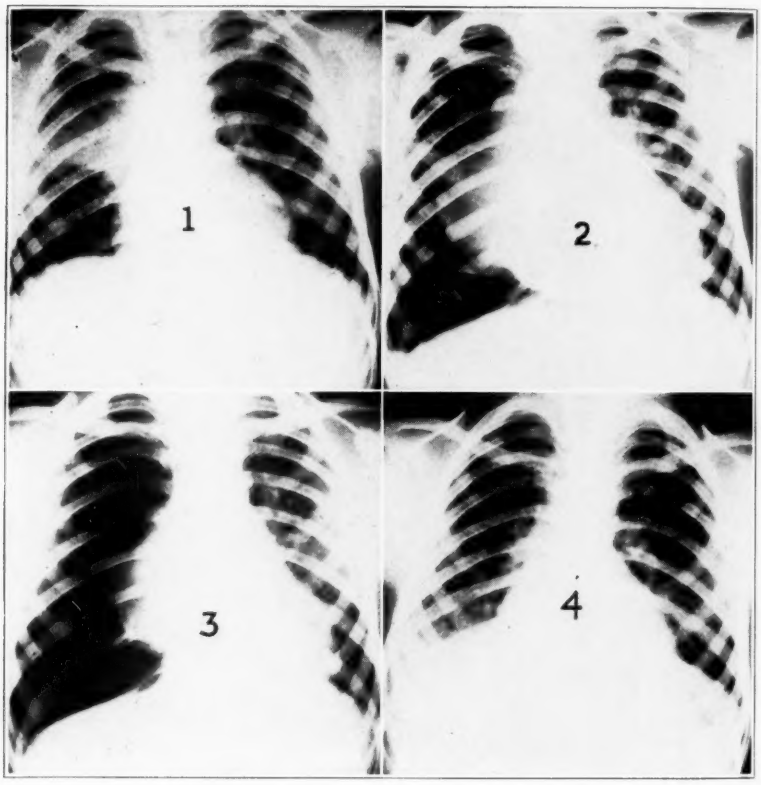

Fig. 6 (case 11).—Serial roentgenograms, showing: *1,* the condition before treatment, with early infiltration; *2,* fair collapse after 750 cc. of air was injected during the first ten hours of therapy (note the small adhesion holding out the lower lobe of the right lung); *3,* more collapse in spite of the persisting adhesion, and *4,* reexpansion nearly complete on the twenty-fifth day, with a small pleural effusion.

fluid increased. The patients were transferred to the surgical service for thoracotomy, and all eventually made a full recovery. The case of one of the patients with empyema is reported, with studies of the lung volume, in another paper.[4]

The possibility that the empyema was a result of puncture of the lung due to faulty technic in performing the pneumothorax should be considered. No error in technic was recognized at the time of thoracentesis. For one patient there was a roentgenologic diagnosis of mediastinal pleural effusion before pneumothorax was initiated, and three cultures of the blood of another yielded Pneumococcus type I.

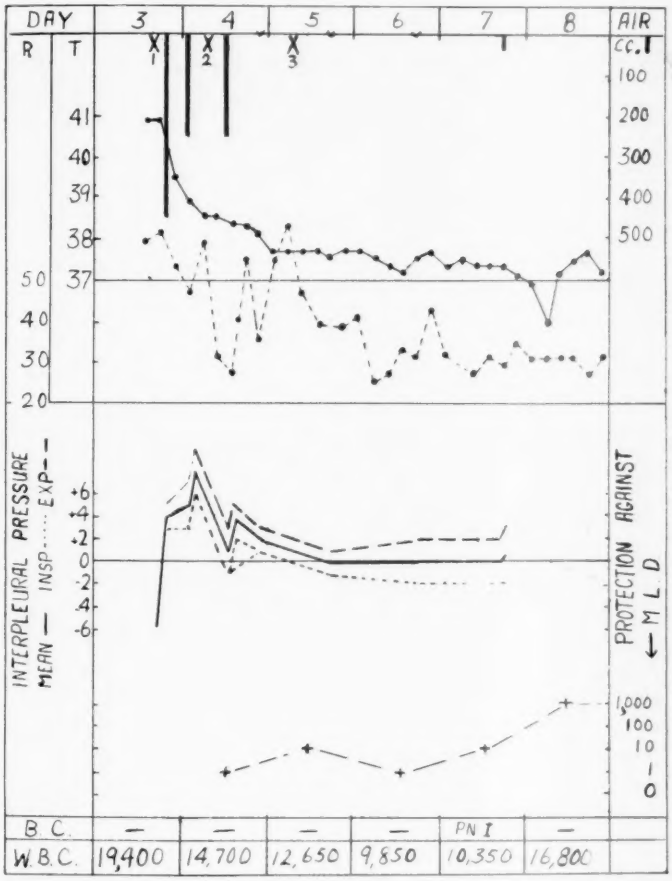

Fig. 7 (case 1).—A boy, 11 years old, had pneumonia, with involvement of the upper lobe of the right lung. Pneumococcus type I and H. influenzae were recovered.

The incidence of empyema during the year in this service has been less than that for the preceding year, when pneumothorax was not used. I do not imply that this was due to benefit resulting from the pneumothorax; it was rather the result of the yearly variation in the incidence of empyema.

The patients with preexisting fibrous adhesions will be considered with other children having adhesions. Here it will suffice to state that the adhesions in these four children prevented collapse to such an extent that the effect of pneumothorax compression therapy could not be fairly evaluated.

Table 3 summarizes the data from the fifteen cases in which evaluation of results, although difficult, is possible. The difficulties arise from

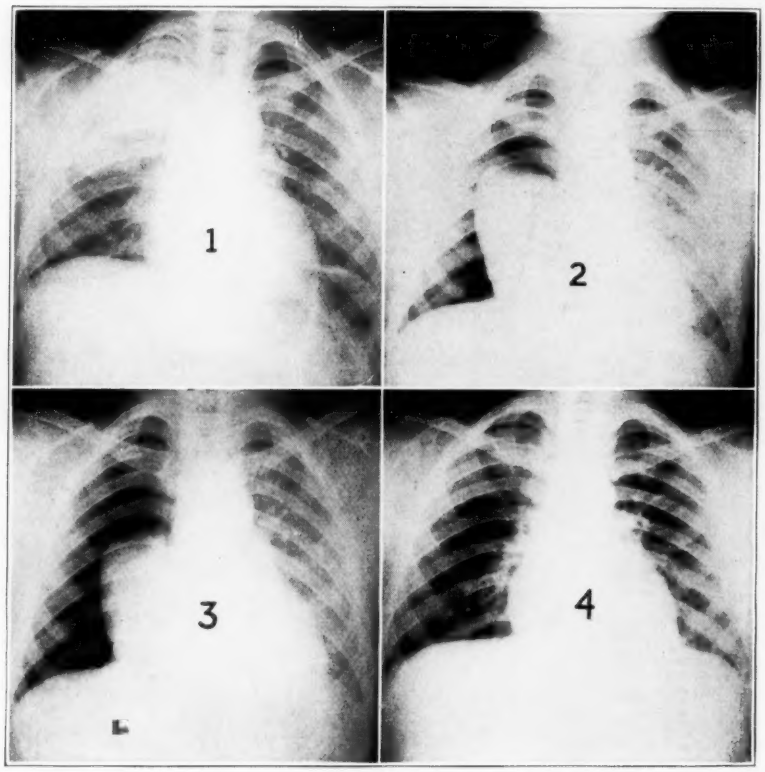

Fig. 8 (case 1).—Serial roentgenograms, showing: *1*, the condition before treatment (the plate was underexposed); *2*, partial collapse after 700 cc. of air was injected during the first eight hours of therapy; *3*, more collapse twenty-four hours later, and *4* reexpansion two weeks after discharge and on the thirty-second day after the onset.

the variation in technic as the study progressed and the variables involved in any clinical study. Three patients were given the first injections of air on the second day of illness, ten on the third day and two on the fourth day. While the history established the time of onset of pneumonia in most of the cases, there were a few in which this

could not be done with certainty. The cases are therefore arranged according to the hours after the initiation of pneumothorax that fever subsided. One patient became afebrile within twenty-four hours, one within thirty-six hours, four within forty-eight hours, four within sixty hours and five later than sixty hours.

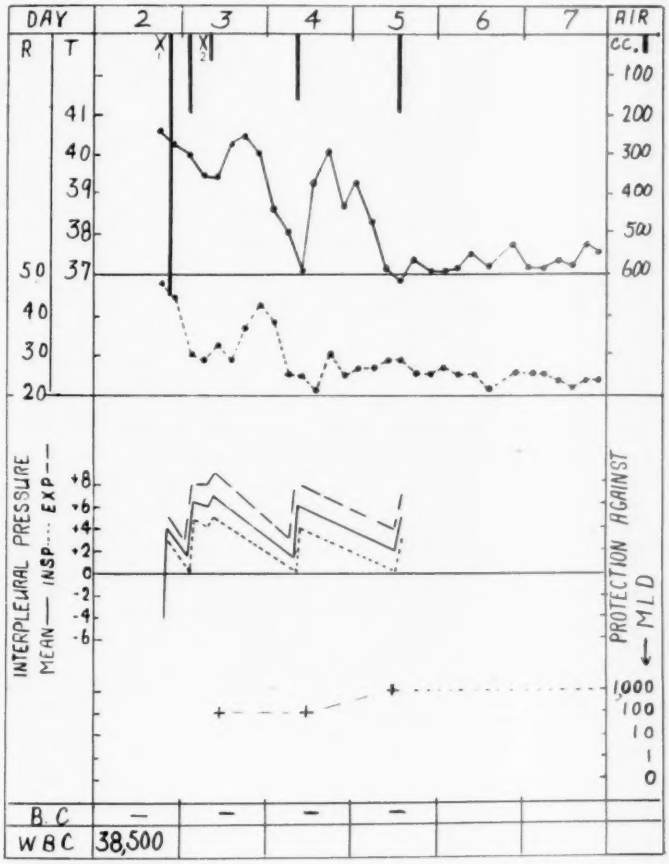

Fig. 9 (case 20).—A girl, 6 years old, had pneumonia, with involvement of the lower lobe of the left lung. Pneumococcus type I and H. influenzae were recovered.

A more detailed consideration of the five children who became afebrile later than sixty hours after the initial thoracentesis will be of value. Treatment was begun in case 18 when the pneumonic infiltration was in the early stage. Compression was rapid. Defervescence occurred by lysis over a period of seventy-two hours. Case 21 (figs. 11 and 12) has already been mentioned as one difficult for the evalua-

tion of results on account of otitis media. Cases 2 and 5 (figs. 1 to 4) have been mentioned as representing early failure under the section on speed of injection of air and interpleural pressure. In case 8 severe acidosis developed on the patient's second day in the hospital, the amount of fluid and calories administered having been inadequate, partly as a result of drowsiness following the frequent administration of tri-bromethanol.

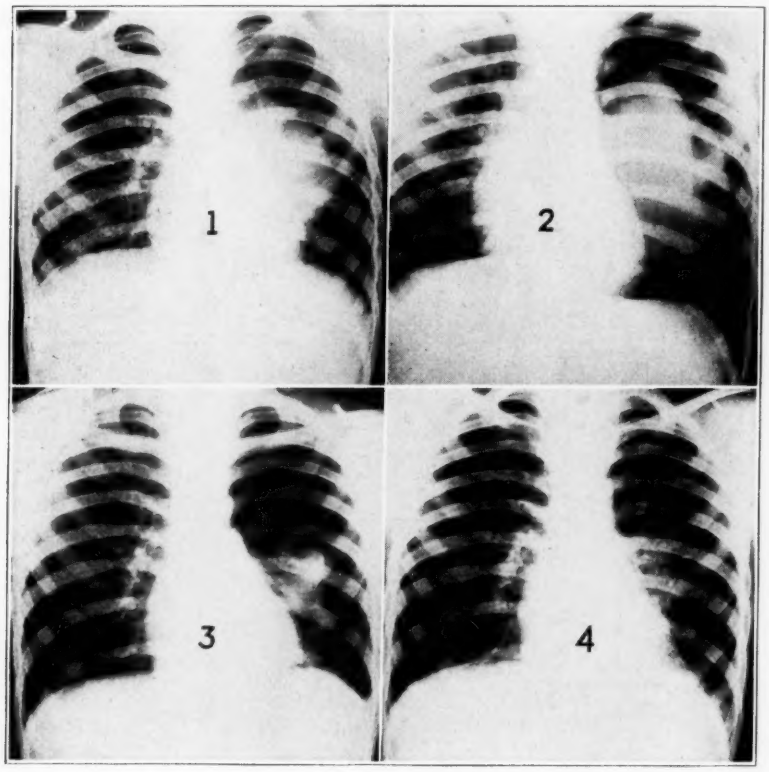

Fig. 10 (case 20).—Serial roentgenograms, showing: *1*, the condition before treatment with a fan-shaped infiltration; *2*, partial collapse, with more air needed, after 850 cc. of air was injected during the first six hours of therapy; *3* nearly complete collapse on the tenth day, before air was withdrawn to hasten reexpansion, and *4*, reexpansion well advanced on the fourteenth day after the removal of 400 cc. of air.

The degree of collapse, as indicated in table 3, was estimated from the roentgenograms as poor, fair or good. The lack of sufficiently frequent roentgen examination offers a difficulty; thus, a patient whose roentgenograms showed fair collapse after the initiation of pneumothorax might have had good collapse in another eighteen hours, but it could not be so recorded if the next film was made at the end of sixty

TABLE 3.—*Cases Without Preexisting Fibrous Pleural Adhesions or Empyema*

Case*	Age, Yr.	Bacteria	Blood Culture	Site		First Treatment			Second Treatment		All Later Treatment			Total Treatments		Result			Collapse,† Hours after First Injection of Air	Comment
				Side	Lobe	Day	Hours after Onset	Air, Cc.	Interval, Hr.	Air, Cc.	Number	Intervals, Hr.	Air, Cc.	Number	Air, Cc.	Recovery	Hours after First Treatment	Day of Disease		
1	11	P. I, H. inf.	+	R	U	3	68	450	7	250	4	12-48	350	6	1,050	Crisis	24	4	Good: 15 hr.	
15	6	P. I, H. inf.	—	L	L	3	54	400	4	150	4	4-10	750	6	1,300	Crisis	36	4	Fair: 3 hr.	
6	2½	P. IV, H. inf.	—	R	L	4	72	100	5	200	3	10-24	600	5	900	Crisis	48	6	Fair to good: 36 hr.	
10	8	P. I, H. inf.	—	R	U	3	48	250	10	300	6	5-48	1,000	8	1,550	Crisis	48	5	Fair: 36 hr.; good: 60 hr.	
11	5	P. I	—	R	U	3	42	400	4	150	8	5-24	850	10	1,400	Crisis	48	5	Fair to good: 20 hr.	
4	5	P. I	—	I. R	L L	4	86	200	48	75	0	.....	...	2	275	Crisis	48	6	Bilateral	
16	5	‡	—	L	L	3	48	475	4	100	7	4-16	775	9	1,350	Lysis	56	5	Good: 16 hr.	Otitis media and mastoiditis
19	1, 3 mo.	P. IV, H. inf.	—	R R	U L	3	48	150	4	125	1	6	100	3	375	Crisis	56	5	Poor: 5 hr.; fair later	
20	6	P. I, H. inf.	..	L	L	2	44	650	4	200	3	6-30	450	5	1,300	Crisis	56	5	Fair: 12 hr.	
17	8	P. I, H. inf.	—	R	U	3	48	600	4	325	2	4- 8	400	4	1,325	Crisis	60	5	Poor to fair: 4 hr.; fair: 20 hr.	
18	5	P. I, H. inf.	—	L	L	3	52	500	4	200	3	6-20	350	5	1,050	Lysis	72	6	Fair: 15 hr.; good: 60 hr.	
21	8	P. I	—	R	L	3	54	650	4	250	3	4-26	375	5	1,275	Lysis	72	6	Good: 24 hr.	Otitis media
2	7	P. I, H. inf.	—	R	U	2	48	300	6	125	5	12-48	450	7	875	Crisis	100	7	Fair: 16 hr.	Lung reexpanded and formed adhesions
8	8	P. I, H. inf.	—	L	L	2	46	450	5	150	6	6-24	700	8	1,300	Lysis	108	7	Fair: 16 hr.	Severe acidosis
5	4	P. I, H. inf.	—	R	U	3	50	150	8	50	5	10-30	500	7	700	Crisis	114	8	Poor: 15 hr.	Inadequate injection of air

* The cases are arranged according to the hour of defervescence after the first injection of air.
† Collapse was determined from roentgenograms.
‡ Type III pneumococcus was obtained from the aural discharge and none from material from the nose or throat.

hours. Likewise, a patient who had good collapse at sixty hours may have had only from poor to fair compression during the first twenty-four hours. With these limitations in mind, a direct relation is seen between the hour of defervescence and the degree of early collapse in the uncomplicated cases. It should be emphasized that in the cases in which early defervescence occurred collapse was not only good but

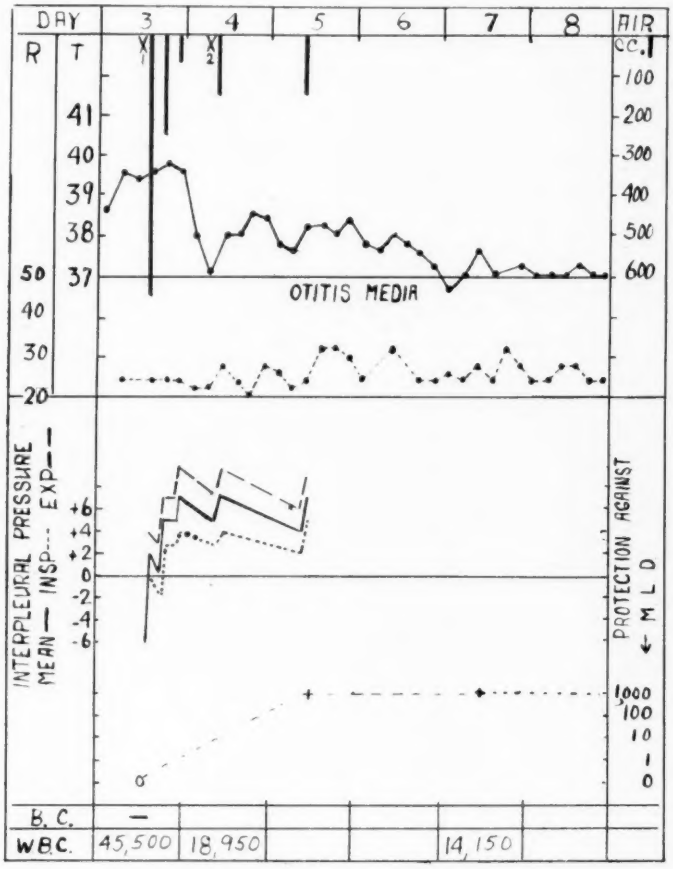

Fig. 11 (case 21).—A girl, 8 years old, had pneumonia, with involvement of the lower lobe of the right lung. Pneumococcus type I was recovered.

rapid, so that the lung was well compressed within from twenty to thirty hours of the initiation of pneumothorax. In order to obtain early collapse it was necessary to raise the interpleural pressure to positive levels rapidly and to maintain it. The degree of pressure needed to compress the lung varied with the age of the child and with the extent of the pneumonic infiltration. The patients were so few that the fol-

lowing figures are only suggestive: From fair to good collapse was obtained in one patient under 3 years of age with a mean pressure of + 2 cm. of water, in five patients from 4 to 6 years of age with a mean pressure of from + 4 to + 5 cm. of water and in five older children with a mean pressure between + 5 and + 7 cm. of water. To obtain such levels of pressure rapidly it was necessary to introduce a large amount of air at a slow rate during the first twelve to eighteen hours.

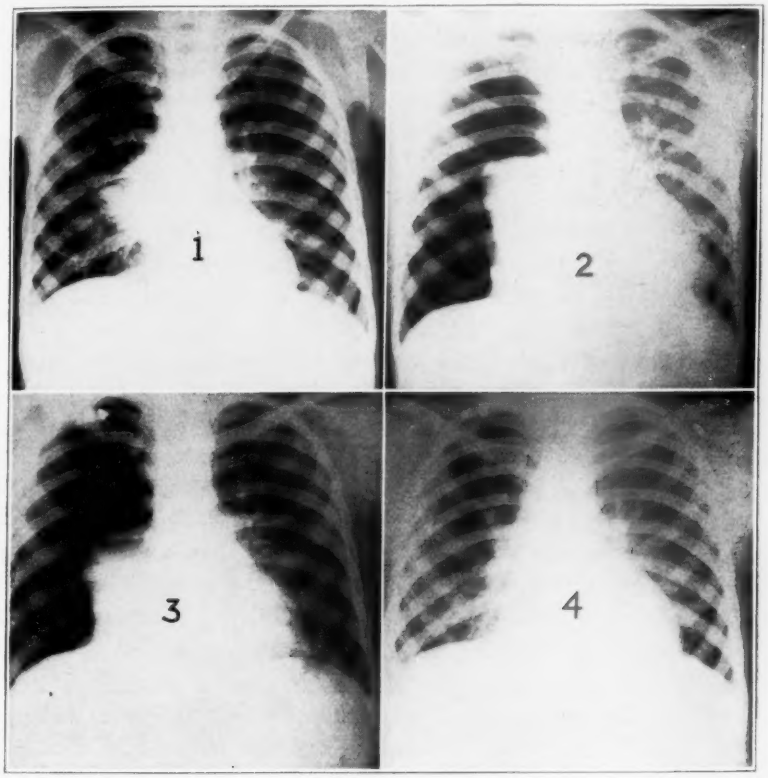

Fig. 12 (case 21).—Serial roentgenograms, showing: *1*, the condition before treatment; *2*, after 975 cc. of air was injected during the first ten hours of therapy; *3*, compression maintained on the ninth day, and *4*, reexpansion twelve days after discharge and twenty-five days after the onset.

In the last four patients, aged 15 months and 6, 8 and 13 years, the volume of air injected on the initiation of pneumothorax was, respectively, 150, 650, 650 and 850 cc., injected at a rate of from 7 to 9 cc. per minute. The average interval between the first and the second injection was four and three-tenths hours. Rapid and satisfactory compression was obtained in all except the 15 month old child, in whom the

interpleural pressure was not raised beyond 0 during the first twelve hours.

By the time 200 cc. of air had been injected the patients who had pleural pain obtained remarkable relief. In most patients the respiratory rate, which had been rapid, became somewhat slower, and the respiration, which had been shallow, showed increased depth, the latter observation being confirmed by the difference in interpleural pressure. As the pressure was slowly pushed to the levels suggested for his age, the patient would eventually complain of shortness of breath, even though dyspnea had been temporarily relieved at the onset of the injection of air. Cyanosis, if present, was usually not increased beyond that obtaining before treatment was begun. Physical examination of the trachea and apex of the heart at this time usually revealed a beginning shift of the mediastinum, and the combination was ordinarily taken as a warning to stop the injection of air. In all cases the signs of acute respiratory embarrassment passed off during the first few hours after the end of an injection. At the time of the first and second injections for refilling, the pressure was carried to higher levels without the appearance of disturbing symptoms.

Often during the latter part of the initial injection of air the patient's face, which had been pale and worried, became flushed and perspiration began to appear. Observers occasionally commented on the improved appearance. It is probable, however, that part of the immediate improvement in color was due to increased venous pressure, which could be observed in the full and pulsating external jugular veins as the injection of air progressed. Otherwise, the patients continued to look actively ill as long as the vital signs were elevated and showed the usual improvement after defervescence, except that during the first few days of complete collapse dyspnea was easily induced. Studies of lung volume, reported in another paper,[4] showed a reduction of subtidal and total volume early in the disease as compared with values during convalescence. The volumes were further reduced by pneumothorax, so that during complete collapse they became about half those noted during convalescence. In brief, the patient had approximately the respiratory capacity of one lung. This gave little or no symptomatic disturbance so long as the patient remained at rest. When, however, activity occurred, especially of a kind to call on the respiratory reserve, as does coughing, the narrowed margin of respiratory safety became apparent, chiefly in the form of dyspnea. This was never severe enough to cause alarm, although a few patients were apprehensive, especially during an episode of coughing.

Five patients were put into an oxygen tent for a brief period, although there was no urgent need for oxygen except in the first patient,

in whom empyema developed, air not being withdrawn rapidly enough to prevent an undue rise in the interpleural pressure.

The average length of hospitalization was less than two weeks in the cases in which the condition was uncomplicated. The average time of defervescence (from the date of onset) for all patients except the three with empyema was five and eight-tenths days. In a recent series of fifty-three cases of lobar pneumonia caused by Pneumococcus type I from this service (in which pneumothorax was not done) the average time of crisis was eight and five-tenths days. Holt gave the average day of crisis in five hundred and sixty-seven cases of lobar pneumonia as seven and one-tenth days.[6]

The importance of early induction of pneumothorax cannot be overemphasized. Rapid collapse was not possible once the roentgenogram showed the pneumonic infiltration to be diffuse throughout an entire lobe (fig. 4). The fact that eighteen of the twenty-two children were admitted to the hospital on the third or fourth day of pneumonia points to the importance of early diagnosis and hospitalization.

ADHESIONS

Adhesions may be suspected from the history or because of difficulty in performing pneumothorax, but it can be diagnosed only by roentgenograms after the adequate injection of air. For therapeutic reasons, which will be discussed, it is important to distinguish between preexisting fibrous adhesions and temporary adhesions formed after pneumothorax is instituted. The adhesions observed in the first roentgenograms made with the patient in the erect position after the institution of pneumothorax which were fairly extensive and which persisted were classified as preexisting and fibrous; those observed in the first roentgenograms made after the institution of pneumothorax which were of slight extent and uncertain persistence were considered as probably preexisting and fibrous, while those which were demonstrated to have formed after pneumothorax was initiated and later to have broken completely or in part were called temporary adhesions. The data for all patients with adhesions are presented in table 4.

The cases are arranged in inverse order according to the time of defervescence after the initiation of pneumothorax. In spite of exceptions, it is apparent that here also the success of pneumothorax therapy was directly related to the degree of collapse attained, which was of course inversely proportional to the extent of the adhesions. In the four patients whose adhesions were classified as preexisting, the collapse attained was from poor to fair, and the time of defervescence was

6. Holt, L. E., and Howland, John: Diseases of Infancy and Childhood, ed. 10, New York, D. Appleton-Century Company, 1933, p. 429.

seventy-two hours or more. It was believed that pneumothorax was either of no value in these patients or could not be evaluated, and the cases have therefore been considered in table 2 together with those of the children in whom empyema developed. Of these four children, two gave a history of pneumonia and two did not. All gave a negative reaction to tuberculin. The available evidence suggests that when preexisting fibrous adhesions are present to an extent to prevent good collapse, pneumothorax should probably be discontinued.

The situation is different when temporary adhesions develop during the course of artificial pneumothorax. The patient in case 2 (fig. 2) presented the best roentgen evidence of this form of adhesion. As

TABLE 4.—*Cases with Adhesions Demonstrable by Roentgenogram*

Case	Age, Years	History of Pneumonia Previously	Nature of Adhesions	Degree of Collapse	Defervescence Hour after First Injection of Air	Comment
7	1 yr., 11 mo.	1933	Preexisting, fibrous	Poor	Lysis: 108 hr.	
12	15	None	Preexisting, fibrous	Poor	Lysis: 108 hr.	
2	7	None	Temporary	Poor	Crisis: 100 hr.	Adhesions broke on fifth day
22	13	None	Preexisting, fibrous	Poor to fair	Lysis: 96 hr.	
14	14	1927	Preexisting, fibrous	Poor to fair	Crisis: 72 hr.	
19	1 yr., 3 mo.	None	Indeterminate	Poor*	Crisis: 56 hr.	
16	5	None	Probably preexisting	Fair to good	Lysis: 56 hr.	
11	5	None	Probably preexisting	Fair to good	Crisis: 48 hr.	
15	6	None	Temporary	Fair to good	Crisis: 36 hr.	Adhesions broke

* Poor collapse was due to inadequate establishment of pneumothorax. The extent of the adhesions was not determined.

already noted, the initial injection of air was carried out in the early stage of the disease, at which time infiltration was limited to the lower part of the upper lobe of the right lung. After a total of 425 cc. of air was injected, a roentgenogram showed fair collapse, with no evidence of adhesions. An insufficient amount of air was given to maintain the early collapse, the interpleural pressure fell to negative levels, the lung reexpanded and adhesions were formed (fig. 2, 3). Enough air was then injected to maintain the mean interpleural pressure at about +1 cm. of water. After five days the adhesions broke and collapse occurred. When temporary adhesions occur, it seems rational to maintain the interpleural pressure at a positive level to favor separation and to decrease the danger of permanent adhesions developing from the temporary ones. The formation of temporary adhesions seems to be favored by severe episodes of coughing during the stage of active collapse. Such temporary adhesions could probably be prevented by the

maintenance of adequate interpleural pressure to prevent reexpansion until the active pneumonic process has subsided. Prevention of cough by slow injection of air and by the administration of codeine or other drugs would also be helpful.

The possibility of the formation of permanent adhesions after the pneumonic process has subsided and reexpansion has occurred should be considered. Such an event would be a possible contraindication to the institution of pneumothorax. The problem might have been settled by waiting until reexpansion was complete and then by instituting pneumothorax a second time to determine the presence or absence of adhesions, but it was felt that such a procedure was not justified. Accordingly, an experiment was carried out in four monkeys, and the data are given in table 5.

TABLE 5.—*Repeated Pneumothorax in Monkeys to Determine if Adhesions Resulted from the First Injection of Air*

Monkey	Weight, Gm.	Date of First Injection of Air	Extent of Collapse	Date of Complete Reexpansion	Date of Second Injection of Air	Extent of Collapse	Adhesions
VI	1,330	1/30/35	Good	2/ 8/35	3/21/35	Complete	None
VII	2,400	2/ 1/35	Good	2/15/35	3/21/35	Complete	None
VIII	2,200	2/ 1/35	Fair	2/15/35	3/29/35	Complete	None
IX	2,200	2/ 8/35	Good	3/12/35	3/21/35	Complete	None

TABLE 6.—*Age, Interpleural Pressure and Mediastinal Herniation*

Case	Age	Estimated Interpleural Pressure When Hernia Was First Noted	Size of Hernia in Cm.* to Left or Right of Vertebral Column When First Noted
19	15 months	+0.5	1.2
7	23 months	+1.0	1.6
5	4 years	+1.0	0.7
18	5 years	+6.0	1.0
11	5 years	+4.0	1.0
15	6 years	+7.0	2.3
17	8 years	+6.0	1.5
14	14 years	+7.0	1.0

* This was measured on roentgenograms from the lateral edge of the vertebral column.

The work demonstrated that it is easy to perform pneumothorax on small monkeys and that the animals tolerate the procedure well, and as far as the data go the observations lend support to the opinion that pneumothorax does not tend to cause permanent adhesions. This opinion gains further strength from the demonstrable breaking of temporary adhesions in the two children whose cases are listed in table 4.

MEDIASTINAL HERNIATION

Herniation of the pleura through the mediastinum was observed in eight patients. As will be noted in table 6, herniation occurred more frequently in children in the low age groups, and the younger the patient

the lower the mean interpleural pressure necessary to cause herniation. In each case the pleural sac herniated through the anterior portion of the mediastinum just under the sternum. In one case there was also herniation in the posterior portion, just in front of the vertebral column. In six cases the herniation was from right to left; in two, from left to right. Pneumothorax therapy was discontinued as soon as herniation was observed, except in two children. In one (case 17) the first appearance of herniation was overlooked on the wet film, and 700 cc. more air was given. During this period the interpleural pressure was increased from a mean of +6 to +9 cm. of water, and the hernia increased in size so that from an original position 1.5 cm. to the left of the sternum it finally extended 3.5 cm. to the left of the sternum. No harmful effects were noted in this or any of the other cases.

It was observed that in two thirds of the cases the lobes which were the seat of the pneumonia were compressed more slowly than the uninvolved lobes. Contrariwise, during reexpansion the change in the involved lobes lagged behind that in the lobes which had not been involved. This was interpreted not as evidence of selective collapse but rather as indicating that lung tissue which is the seat of a pneumonic process is less responsive to changes in interpleural pressure than is normal tissue.

Shift of the mediastinum away from the treated side was demonstrable by roentgenogram and by physical examination in nearly all cases. In more than half the children the shift was slight, and in only about a fourth of the cases was it marked. These considerable shifts of the mediastinum were observed only within the first few hours after the injection of large amounts of air. Subsequently, films showed a return of the mediastinum toward a position in the midline, apparently attained by gradual collapse of the diseased lung, by circulatory changes, by the absorption of air and by the maintenance of the treated side of the chest in a position of complete expansion, with the diaphragm depressed.

Over 90 per cent of the patients showed an effusion on the side of the pneumothorax at one time or another. Usually the amount of fluid was so slight as to fill only a small part of the costophrenic space, but in two children the level of the fluid extended to the fifth and fourth ribs, respectively. In nearly every case the effusion was absorbed by the time reexpansion was complete, but in case 12 the effusion persisted for more than a month after the patient became afebrile and then resolved completely.

BACTERIOLOGIC AND SEROLOGIC DATA

As may be seen in table 7, there were fifteen children with Pneumococcus type I in material from the nose or throat and three more with

TABLE 7.—*Bacteriologic and Serologic Data*

Case	P. I	P. I Antibodies in Serum but Not in Nose or Throat	Other Types of Pneumococcus	H. Influenzae	Appearance of Protective Bodies, Day of Disease*											
					2	3	4	5	6	7	8	9	10	11-14	14-21	21
9†	+	.....	.....	..	..	..	0	..	++++	..	..	..	..	++++	++++	..
4	+	.....	.....	..	..	..	..	..	‡	++++	++++	..	..	++++	..	..
12	+	.....	.....	..	..	0	0	..	++	..	‡	..	++++	..	++++	++++
3†	+	.....	.....	..	..	0	0	0	..	0	±	+++	..	..	..	±
11	..	+	.....	..	..	..	..	+++‡	++++	..	..	..	++++	++++	..	..
14	..	+	.....	..	..	0	..	..	++‡	++++	++++	..	..	..	++	..
21	..	+	.....	..	..	0	..	++++	‡	++++	..	++++	..	..	..	..
2	+	.....	.....	+	..	0	++	..	++++‡	++++	..	..	..	..	..	++++
8	+	.....	.....	+	..	..	..	..	..	..	..	..	..	..	..	..
15	+	.....	.....	+	..	..	++++‡	++++	..	++++	..	..	..	++++	..	..
18	+	.....	.....	+	..	0	+++	..	..	++++‡	++++	..	++++	++++	..	..
20	+	.....	.....	+	..	+++	+++	++++‡	..	..	++++	..	++++	..	..	..
13†	+	.....	.....	+	..	0	..	++++	..	..	++++	..	..	++	++	..
17	+	.....	.....	+	..	..	++	++++‡	..	..	++++	++++	..	++++	..	..
1	+	.....	VIII	+	..	..	+‡	++	+	++	++++	++++	..	+++	..	0§
7	+	.....	XVIII	..	..	0	..	0	..	+	‡	..	0	++++	++++	§
10	+	.....	III	+	..	..	+++	++++‡	..	++++	++++	..	++++	..	++++	§
5	+	.....	VIa	+	..	..	+++	..	+++	+++	+++‡	++	..	..	..	§
19	..	.....	Unclassified	+	..	..	..	..	..	..	..	..	..	..	..	..
16	..	.....	‖	..	..	..	..	..	..	..	..	..	..	..	..	..
22	..	.....	XIV	..	..	..	..	..	..	..	..	..	..	..	..	..
6	..	.....	IV	+	..	..	±	+++	‡	+++	..	++++	..	++++	..	..

* 0 means no protective bodies; +, protection against 1 M.L.D. of a homologous, virulent pneumococcus; ++, protection against 10 M.L.D.; +++, protection against 100 M.L.D., and ++++, protection against 1,000 M.L.D.

† Empyema was present.

‡ The patient was afebrile after this day.

§ The protection test was made with Pneumococcus type I.

‖ Pneumococcus type III was obtained from the ear and none from the nose or throat.

type I antibodies in the blood serum after recovery but with pneumococcus not obtained from material from the nose or throat. Among the patients with Pneumococcus type I were ten who also had H. influenzae in the nose or throat. Cultures of the blood of three patients gave positive results, with empyema developing in one. Pneumococcus type I was recovered from the pleural exudate of the three patients with empyema, and the exudate of one child also yielded the influenza bacillus. The time of appearance of humoral antibodies was determined by mouse protection tests in eighteen patients. The difficulty of collecting blood made daily tests impossible. The average time of appearance of antibodies in the blood was on the day preceding the fall of the temperature to normal.

SUMMARY AND CONCLUSIONS

Artificial pneumothorax was instituted without fatality in the treatment of twenty-two children with lobar pneumonia from 15 months to 15 years of age. Most children required sedatives, and for this purpose morphine gave excellent results. A rise in the interpleural pressure averaging + 4 cm. of water was observed when patients who had been lying on their sides during the injection of air were turned to lie on their backs. Since the extent of the rise varied with the age and other factors, it semed best to treat the children in the supine position. It must therefore be remembered in comparing my data with those of other authors that the readings of interpleural pressure are from 0 to + 7 cm. of water higher than they would be if the patients had been lying on their sides, with the collapsed lungs upward.

In general, the results of compression of the pneumonic lung were encouraging when early and good collapse was obtained and were of doubtful value when compression was either delayed or incomplete. More complete and rapid compression of the lung without discomfort to the patient was obtained by decreasing the rate of injection of air used in the early cases to a speed of from 7 to 9 cc. of air per minute but at the same time increasing the amount of air, especially on the initiation of pneumothorax. My observations, although limited, suggested that the interpleural pressure needed to give early and good collapse varies both with the age of the child and with the extent of the pneumonic infiltration. Tentative levels of pressure are suggested which gave satisfactory collapse in children under 3 years, between 4 and 6 years and older than 6 years. The interpleural pressure was pushed slowly toward these tentative levels, with reliance on the symptomatology, especially beginning dyspnea, and on evidence of mediastinal shift for warning to stop. In all cases respiratory distress passed away within a few hours. At the first renewal of air, given after an interval

of about four hours, the pressure was carried to higher levels without causing disturbing symptoms.

Certain difficulties should be mentioned. After pneumothorax had been established, the usual physical signs were so obscured or altered that it was necessary to rely on the roentgenogram to follow the extent of the collapse and the course of the pneumonia. Roentgen examination was also necessary for the diagnosis of mediastinal hernia and of adhesions, particularly to differentiate between preexisting fibrous pleural adhesions and temporary adhesions formed during the course of pneumothorax. In addition to this dependence on the roentgenogram, consideration should be given to the amount of time which the procedure requires and to the usual technical requirements for performing pneumothorax. Furthermore, experience showed the importance of initiating pneumothorax before the pneumonic infiltration had become diffuse. This was not always easy, since a patient was rarely admitted to the hospital before the third day of pneumonia.

This work does not establish the value of artificial pneumothorax therapy in lobar pneumonia of children. A technic has been developed, however, for the therapeutic use of this procedure, which when satisfactorily carried out gave encouraging results. In evaluating the results it would be well to keep in mind that the technic developed as the work progressed and that future patients should benefit from the technical improvements. The therapeutic value of the procedure is still a clinical and an experimental problem.

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IMMUNE REACTIONS INDUCED IN INFANTS BY INTESTINAL ABSORPTION OF INCOMPLETELY DIGESTED COW'S MILK PROTEIN

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There seems no reason to doubt that intestinal proteolysis is designed to disrupt the protein molecule completely into its constituent amino-acids before absorption occurs.

It has long been recognized, however, that under the influence of disease or through procedures in the experimental laboratory protein not completely digested may be absorbed from the intestine and enter the body fluids. Most of the earlier observations were made on experimental animals, but it also was demonstrated that such absorption may occur in infants who have nutritional disorders or are fed excessive amounts of protein foods.

The earlier literature was reviewed by Lawatschek,[1] Moro,[2] Bauer,[3] Ascoli and Vigano,[4] Michaelis and Oppenheimer,[5] Ganghofner and Langer,[6] Hamberger and Sperk,[7] Lust,[8] Hayashi,[9] Schloss and

From the New York Hospital, and the Department of Pediatrics, Cornell University Medical College.

1. Lawatschek, R.: Die enterale Resorption von genuinem Eiweiss bei Neugeborenen und darmkranken Säuglingen, Prag. med. Wchnschr. **39**:185, 1914.

2. Moro, E.: Kuhmilchpräcipitin im Blute eines 4½ Monate alten Atrophikers, München. med. Wchnschr. **5**:214, 1906.

3. Bauer, J.: Ueber die Durchgängigkeit des Magendarmkanals für Eiweiss und Immunkörper und deren Bedeutung für die Physiologie und Pathologie des Säuglings, Arch. f. Kinderh. **42**:399, 1905; Ueber den Nachweis der präcipitablen Substanz der Kuhmilch im Blute atrophischer Säuglinge, Berl. klin. Wchnschr. **43**:711, 1906.

4. Ascoli, M., and Vigano, L.: Zur Kenntnis der Resorption der Eiweisskörper, Ztschr. f. physiol. Chem. **39**:283, 1903.

5. Michaelis, L., and Oppenheimer, C.: Ueber Immunität gegen Eiweisskörper, Arch. f. Anat. u. Physiol., supp., 1902, p. 336.

6. Ganghofner, K., and Langer, J.: Ueber die Resorption genuiner Eiweisskörper im Magendarmkanal neugeborener Tiere und Säuglinge, München. med. Wchnschr. **51**:1497, 1904.

7. Hamberger, F., and Sperk, B.: Biologische Untersuchungen über Eiweissresorption vom Darm aus, Wien. klin. Wchnschr. **17**:641, 1904.

8. Lust, F.: Die Durchlässigkeit des Magendarmkanals für heterologes Eiweiss bei Ernährungsgestörten Säuglingen, Jahrb. f. Kinderh. **77**:383, 1913.

9. Hayashi, J.: Ueber die Durchlässigkeit des Säuglingsdarmes für artfremdes Eiweiss und Doppelzucker, Monatschr. f. Kinderh. **12**:749, 1913.

Worthen [10] and Anderson and Schloss.[11] Recently the literature was thoroughly reviewed by Ratner and Gruehl.[12]

In 1926 Walzer [13] showed by the delicate test of Prausnitz and Küstner for passive cutaneous sensitization that intestinal absorption of incompletely digested protein may occur in normal adults.[14] Such absorption could not be demonstrated regularly in persons on a normal diet and under normal conditions, but it occurred with comparative regularity when uncooked protein food was ingested by fasting subjects. After a fast of from six to eight hours, 50 Gm. of raw herring or one raw egg white was ingested. In 88 per cent of the subjects, absorption of undigested protein was demonstrated by reaction in a cutaneous area previously sensitized by human serum containing specific sensitizing antibody for the protein ingested. Walzer's observations [14a] demonstrate that the intestinal tract of normal adults is not impermeable to products of protein digestion containing a hapten group, but they do not prove that such absorption occurs with regularity in persons under normal conditions of habit and diet nor do they offer any evidence that protein in antigenic form is thus absorbed.

If significant amounts of antigenic protein are regularly absorbed from the intestines of normal persons, one should be able to demonstrate in the blood the presence of complement-fixing and precipitating antibodies for highly antigenic proteins, such as those of milk and egg, as these antibodies are developed when protein is administered parenterally or is absorbed from the intestinal tract in significant amounts. It is of course conceivable that under entirely normal conditions antigenic protein may be absorbed regularly in amounts too minute to cause the

10. Schloss, O. M., and Worthen, T. W.: The Permeability of the Gastro-Enteric Tract of Infants to Undigested Protein, Am. J. Dis. Child. **11**:342 (May) 1916.

11. Anderson, A. F., and Schloss, O. M.: Allergy to Cow's Milk in Infants with Nutritional Disorders, Am. J. Dis. Child. **26**:451 (Nov.) 1923.

12. Ratner, B., and Gruehl, H. L.: Passage of Proteins Through the Gastro-Intestinal Wall, J. Clin. Investigation **13**:517, 1934.

13. Walzer, M.: A Direct Method of Demonstrating the Absorption of Incompletely Digested Proteins in Normal Human Beings, J. Immunol. **11**:249, 1926.

14. The test of Prausnitz and Küstner for passive cutaneous sensitization is extremely delicate and under favorable conditions can detect protein diluted many million times. Essentially it is a test for the detection of the hapten fraction of protein and when positive does not prove absolutely that complete antigen has been absorbed.

14a. After this article was submitted for publication, Wilson and Walzer (Absorption of Undigested Proteins in Human Beings: IV. Absorption of Unaltered Egg Protein in Infants and in Children, Am. J. Dis. Child. **50**:49 [July] 1935) reported similar observations on a group of children.

appearance of antibodies demonstrable by present methods, but there is no evidence to justify this assumption.

From an immunologic point of view and in possible relation to allergy, the absorption of sufficient amounts of ingested protein to provoke the occurrence of cutaneous sensitivity and the appearance of specific antibodies in the blood would seem to be of special significance. Our own interest in the intestinal absorption of incompletely digested protein has been centered largely on the influences which condition the absorption of amounts sufficient to provoke immunologic response.

In 1925 Anderson, Schloss and Myers [15] published observations demonstrating that when infants and young children were continuously fed a protein which had not previously entered their diet, precipitin specific for the protein fed could be detected in the blood. The precipitin could be detected after the protein was fed for from ten to twenty days. Despite the continued ingestion of the protein, precipitin was present only for a short time and then disappeared. Such experiments were conducted by feeding milk, egg white, sheep serum and almond. It seemed particularly significant that when the different proteins were fed successively to the same infant or child specific precipitin to each appeared in turn, usually after from ten to twenty days, lasted a short time and then could be detected no longer.

During these investigations, DuBois, Anderson and Schloss [16] observed that temporary cutaneous hypersensitiveness to the specific protein developed in 50 per cent of the infants.

The observation that specific precipitin was present in the blood for a short time and then disappeared, despite the continued ingestion of the protein, aroused the suspicion that some mechanism had become operative which inhibited the absorption of protein in antigenic form. Only by such an assumption could one explain the presence and then the disappearance of precipitin during continuous ingestion of the protein.

The significance of these experiments was limited to some extent by the lack of direct evidence of the absorption of antigen.[17] The occurrence

15. Anderson, A. F.; Schloss, O. M., and Myers, C.: The Intestinal Absorption of Antigenic Protein, Proc. Soc. Exper. Biol. & Med. **23**:180, 1925.

16. DuBois, R. O.; Schloss, O. M., and Anderson, A. F.: The Development of Cutaneous Hypersensitiveness Following Intestinal Absorption of Antigenic Protein, Proc. Soc. Exper. Biol. & Med. **23**:176, 1925.

17. We may be using the term antigen erroneously. According to the modern conception, it is possible that a protein derivative detected in the blood stream by reaction with antibodies may contain only a hapten group and therefore, strictly speaking, is not a complete antigen. The fact that its introduction into the circulation is followed by the production of specific antibodies, however, suggests that it is complete. For descriptive purposes, throughout this paper the term "antigen" is used to designate a protein substance capable of reacting with complement-fixation antibodies.

of specific precipitins in the blood following the ingestion of a protein seemed adequate indirect evidence that such protein had been absorbed in antigenic form. These observations, however, did not give direct information concerning the beginning, intensity or duration of the absorption of antigen. This phase of the subject seemed of sufficient importance to warrant further and more complete investigation, which was therefore undertaken by us.

There are three methods for the direct detection of foreign protein in the blood: the precipitin, anaphylactic and complement-fixation tests.[18] The precipitin test is accurate but is capable of detecting only relatively large amounts of protein. This is due to the fact that animal serums cannot be obtained with a sufficiently high precipitin titer to detect minute amounts of protein in the blood serum. This conclusion was reached by Anderson and Schloss after many experiments and variations of technic. The anaphylactic test showed the same limitations.

In preliminary experiments made by us the complement-fixation test proved to be sufficiently sensitive to detect very small amounts of foreign protein in the blood and presented the further advantage of permitting detection of antibody at the same time. This test therefore seemed suitable for the purposes of this investigation.

The data on which this communication is based were derived from a study of specific antigen and antibody in the blood of young infants induced by the continuous feeding of cow's milk.

SUBJECTS AND METHODS

All the subjects were on an adequate diet, and specimens of blood were collected for examination without reference to the time of the previous meal. As controls, older children and adults were chosen whose diets contained at least 1 quart (946 cc.) of milk daily. Similar tests were performed on blood from a group of infants of various ages who were entirely breast fed. The results were uniformly negative and served as a further control on the significance of positive results obtained by the technic employed.

Blood was collected in sterile test tubes and was allowed to clot immediately. Each specimen was tested by complement fixation for the presence of lactalbumin and its specific antibody, as well as for the antibodies against the total milk proteins.

1. *Test for Antigen.*—Natural antisheep amboceptor was absorbed from the human serum by adding 1 drop of packed, washed sheep red blood cells to 2 cc. of whole blood and placing it in the icebox for five minutes. At the end of that time the blood was centrifugated, and the serum was removed and heated at 56 C. for fifteen minutes.

18. The passive sensitization test of Prausnitz and Küstner detects foreign protein in the blood, but for obvious reasons it is not applicable when the protein searched for is ingested every three or four hours over a long period and therefore may be present in the blood continuously.

One-tenth cubic centimeter of human serum was then placed in each of two tubes, to which was added 0.1 cc. of antilactalbumin rabbit serum in dilutions of 1:40 and 1:80, 2 units of complement diluted to 0.1 cc. and physiologic solution of sodium chloride to make 0.4 cc. (Tests were originally made with 0.2, 0.1 and 0.05 cc. of human serum and a total volume of 1 cc. The 0.2 cc. amount was discarded because of frequent anticomplementary reaction and the 0.05 cc. amount because positive results were seldom encountered.)

The tubes were placed in the icebox for eighteen hours. (This was found to produce greater sensitivity than incubation for one hour at 37.5 C.) At the end of eighteen hours the tubes were placed in a water bath at 37.5 C. for ten minutes, and 0.1 cc. of hemolysin dilution (containing 2 units of sheep cell hemolysin) and 0.1 cc. of 2.5 per cent sheep cell suspension were added. The reactions were read after the mixture was thoroughly shaken and incubated at 37.5 C. for one hour.

Preparations for a Complete Test of Fixation of Specific Antigen and Antibody *

	Human Serum	Rabbit Serum 1:40	Rabbit Serum 1:80	Lactalbumin or Skimmed Milk, Dilutions	Dilution of Complement, 2 Units	Physiologic Solution of Sodium Chloride†	Hemolysin Dilution, 2 Units	Red Blood Cells from Sheep, 2.5%
Antigen determination	0.1	0.1	...	...	0.1	0.1	0.1	0.1
	0.1	...	0.1	...	0.1	0.1	0.1	0.1
Antibody determination (10 tubes)	0.1	...	...	0.1	0.1	0.1	0.1	0.1
Human serum, control	0.1	...	...	...	0.1	0.2	0.1	0.1
Rabbit serum, control	...	0.1	...	...	0.1	0.2	0.1	0.1
	...	...	0.1	...	0.1	0.2	0.1	0.1
Antigen, control	...	...	...	0.1	0.1	0.2	0.1	0.1
Hemolytic system, control	...	...	...	...	0.1	0.3	0.1	0.1
Known positive serum control for whole milk	...	0.1	...	0.1	0.1	0.1	0.1	0.1
and lactalbumin antibodies	...	...	0.1	0.1	0.1	0.1	0.1	0.1

* The readings were recorded as follows: 4 plus reaction, no hemolysis (complete fixation of complement); 3 plus reaction, slight hemolysis; 2 plus reaction, about half of cells hemolyzed; 1 plus reaction, almost complete hemolysis, and 0 reaction, complete hemolysis (no fixation of complement).

† The respective constituents, as indicated in the first five columns, were combined and placed in the icebox over night. The constituents indicated in the last two columns were added, and the preparation was incubated at 37.5 C. for one hour.

2. *Test for Antibodies.*—One-tenth cubic centimeter of human serum, absorbed and inactivated as described in the preceding paragraph, was placed in each of ten tubes, and to each was added 2 units of complement diluted to 0.1 cc. To five tubes was added 0.1 cc. of milk powder in dilutions of 1:1,000, 1:5,000, 1:10,000, 1:20,000 and 1:50,000, respectively. To the remaining five tubes, 0.1 cc. of lactalbumin in the same dilutions was added. The volume of the mixture in each tube was then made up to 0.4 cc. with physiologic solution of sodium chloride.

Controls for the human serum to be tested, rabbit immune serum, antigen and the hemolytic system were set up at the same time. Tests for the detection of antibody for lactalbumin and for whole cow's milk in a known positive serum were included.

Fixation and addition of the hemolytic system were then carried out as described in the paragraph on antigen titration.

The final set-up for a complete test is shown in the table.

3. *Preparation of Lactalbumin.*—In the preparation of lactalbumin, fresh certified raw skimmed milk was employed. Casein was removed by the method of Van Slyke and Baker.[19] Globulin was then precipitated by half-saturation with ammonium sulfate and was filtered off.

The remaining filtrate was saturated with ammonium sulfate, and the resultant precipitate was removed by suction in a Buchner funnel. This was washed off the filter paper with a small amount of distilled water and dialyzed in a collodion bag in the icebox. Dialysis was considered complete when the addition of barium chloride to the dialysate failed to indicate the presence of sulfate.

Lactalbumin was precipitated out of the dialysate by dropping small quantities into acetone. After immediate centrifugation, the acetone was poured off, and the product was washed in ether. It was then dried in air and stored in small vials until used. (It is possible that the lactalbumin thus prepared contained traces of lactoglobulin.)

4. *Preparation of Rabbit Immune Serum.*—During the course of the investigation, the serum from three different rabbits was used. The methods of preparation were as follows:

RABBIT F 10.—One-tenth gram of dry lactalbumin dissolved in 2 cc. of saline solution was injected intravenously at intervals of three days for fifteen days. One week later the titer of the serum was 1:100,000. Three similar injections were then given at two day intervals, and the animal was exsanguinated one week later. Diluted 1:40 (one-fourth anticomplementary dose) the serum titer was 1:500,000, and diluted 1:80 the titer was 1:100,000.

RABBIT F 8.—In an attempt to obtain a serum of higher titer, a preliminary series of injections of egg white was administered. Two cubic centimeters of a 1:6 dilution of egg white was injected intravenously every two days for fourteen days. After an interval of two weeks, 0.1 Gm. of lactalbumin dissolved in 2 cc. of saline solution was injected intravenously every two days for fourteen days. Two weeks later the animal was bled to death. After standing in the icebox for some time, the serum had a titer of 1:1,000,000 when used in a dilution of 1:80.

RABBIT F 16.—One-tenth gram of lactalbumin dissolved in 5 cc. of saline solution was injected intravenously every two days for twenty-two days. Sixteen days later the animal was exsanguinated. Diluted 1:40 the titer of the serum was 1:1,000,000, and diluted 1:80 the titer was 1:500,000.

5. *Preservation of Rabbit Immune Serum.*—Natural sheep amboceptor was absorbed by adding 1 drop of packed, washed sheep cells to 2 cc. of whole rabbit blood, the blood being allowed to remain in contact with the sheep cells for five minutes at 3 C. and centrifugated rapidly and the serum inactivated at 56 C. for fifteen minutes.[20]

The serum was then preserved with 50 per cent glycerin, stored in the icebox and used in dilutions equal to one fourth the anticomplementary dose.

6. *Reagents.*—Amboceptor: The sheep cell hemolysin used was obtained from a commercial laboratory and was titrated according to the Kolmer method.

Complement: The complement was obtained from the pooled serum of three guinea-pigs, preserved with 8.5 per cent crystalline sodium chloride and diluted 1:10 with distilled water shortly before use.

19. Van Slyke, L. L., and Baker, J. C.: The Preparation of Pure Casein, J. Biol. Chem. **52**:127, 1918.

20. Kolmer, J. A.: Serum Diagnosis by Complement Fixation, Philadelphia, Lea & Febiger, 1928, p. 388.

Indicator: Sheep blood cells, preserved in solution of formaldehyde, were kept in the icebox until used. Shortly before being used, a sufficient quantity was washed four times in saline solution and made up to a 2.5 per cent suspension.

Reagent Control: The complement and hemolysin were titrated before each group of tests was performed, with 0.1 cc. (2 units) of each reagent.

RESULTS

Direct Detection of Lactalbumin in the Circulating Blood.—A total of 460 complement-fixation tests for the presence of lactalbumin in the circulating blood were performed on 229 normal infants, children and adults varying in age from 1 day to 30 years. None of the subjects included in this group were suffering from, or had recently recovered from, infections or gastro-intestinal disturbances, and all were receiving

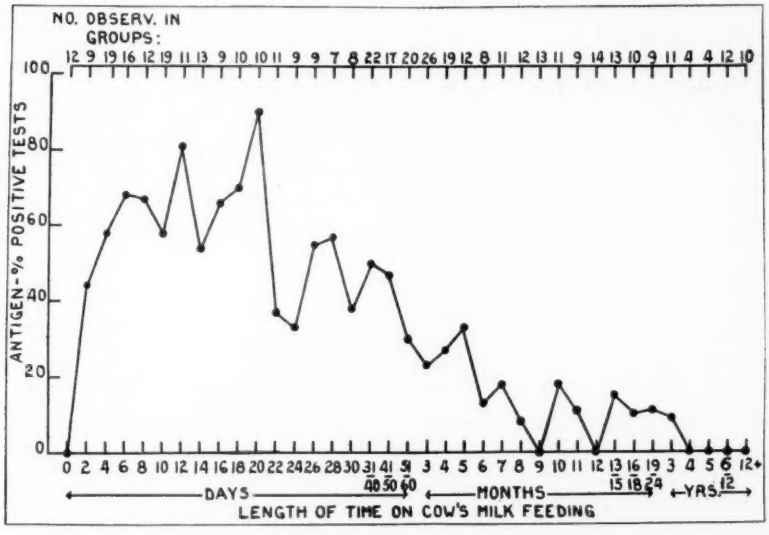

Fig. 1.—Graph showing the percentage of positive reactions for lactalbumin in the blood of subjects receiving cow's milk for various lengths of time.

an ordinary diet for their respective ages. In general, not more than one or two tests were made on any subject, although a few infants were examined at intervals for several months.

Chart 1 shows the number of tests included in each group and the proportion of positive results. It is to be noted that in this and subsequent charts the length of time the subject had been receiving cow's milk, rather than the age, was considered. The fact that many of the infants were several months old before cow's milk was first ingested in no way altered their response.

Analysis of these results reveals that lactalbumin appears in the infant's blood within a few days of its first ingestion, is present in from

60 to 90 per cent of infants on the fourth to the twentieth day and then rapidly diminishes in frequency of appearance. Only in isolated instances is even a weak reaction observed after the fifth month and, with 1 exception, never after the twentieth month.

In the group of infants who were examined repeatedly over periods of weeks or months it was universally noted that in any 1 infant lactalbumin was not constantly present over a certain period of time but appeared intermittently.

Determination of Specific Antibodies for Cow's Milk in the Circulating Blood.—Specimens of blood submitted for examination for lactalbumin were also examined for the presence of the specific complement-fixation antibodies for cow's milk proteins and lactalbumin. In

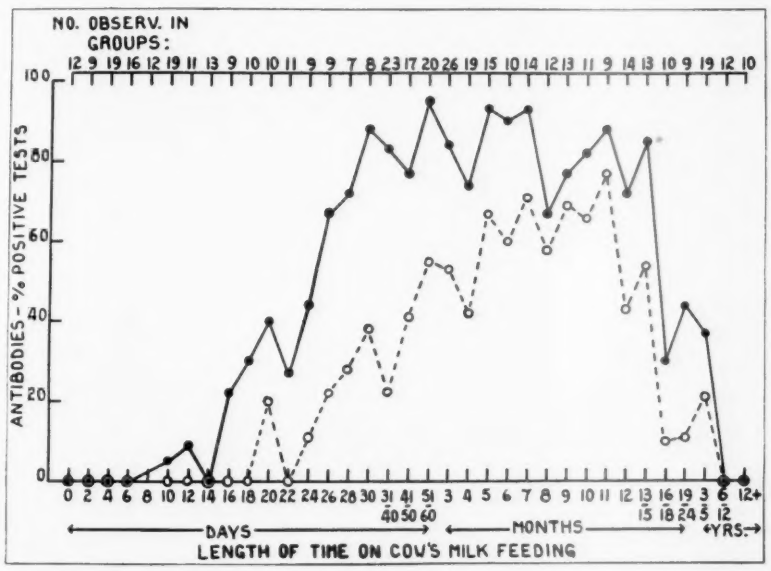

Fig. 2.—Graph showing the percentage of positive reactions for antibodies, detected by skimmed cow's milk (solid line) and by lactalbumin (broken line) in the blood of persons receiving cow's milk for various lengths of time.

all instances the blood was tested for the two antibodies simultaneously.

The interval between the initial ingestion of cow's milk and the appearance of the whole milk antibodies varied between eight and fifty days, but in most instances the interval was between twenty and thirty days. Once established, the antibody was constantly present for several months. No instance was observed in which it disappeared and subsequently reappeared in the blood of a healthy infant.

Chart 2 reveals that antibodies for cow's milk are present in the blood of practically all infants between 1 and 15 months, then the percentage of positive reactions drops precipitously, and only an occa-

sional positive reaction is observed between the second and the fifth year. The isolated positive reactions in the latter group may be due to the absorption of a small amount of antigen during an intestinal disorder or to the persistence of the antibodies long after the last absorption of antigen.

The specific antibody for lactalbumin is slower in appearing than that which is detected by using the sum of the cow's milk proteins as antigens. It was never noted before the twentieth day and seldom before the fortieth.

The period during which a positive reaction for lactalbumin antibody is most frequently observed coincides with that for the total milk protein antibodies. The difference in the percentage of positive results is

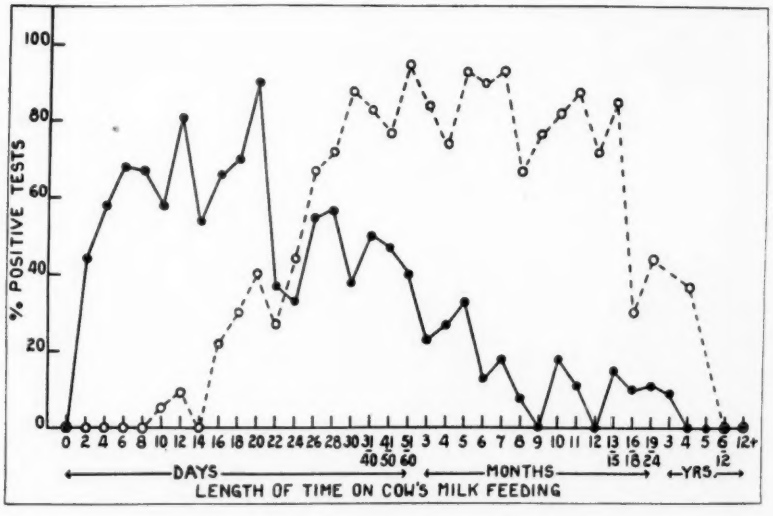

Fig. 3.—A composite graph illustrating the relative incidence of lactalbumin and antibodies for skimmed cow's milk in the blood of subjects receiving cow's milk for various lengths of time. The solid line indicates the antigen and the broken line, the antibody.

probably accounted for by instances in which the infants' blood contained specific antibodies for casein or lactoglobulin and not for lactalbumin. In all subjects followed for several months, however, the lactalbumin antibody appeared at some time. In general, the reactions were not so strongly positive and were more transient than those for the total milk protein. No subject was observed in whom a reaction was positive for the lactalbumin antibody and negative for the whole milk antibodies at the same time.

Comparison of Curves for Antigen and Antibodies.—Lactalbumin is most frequently detected in the circulating blood during the first few

days of ingestion of milk. Coincident with the development of specific antibodies, however, the proportion of subjects in whom it is demonstrable is diminished, and it is only occasionally present during the period of maximum incidence of antibodies. The reciprocal relationship between antigen and antibody is best illustrated by superimposing the curves for the presence of lactalbumin and the antibodies for the protein of cow's milk. The graph in chart 3 shows the relationship strikingly. Lactalbumin, as prepared by us, is probably a less potent antigen than the total proteins of cow's milk. Therefore, a composite graph of the curves for lactalbumin and lactalbumin antibody is less striking.

The time of absolute disappearance of the antigen invariably anteceded the disappearance of antibody from the circulating blood. Neither

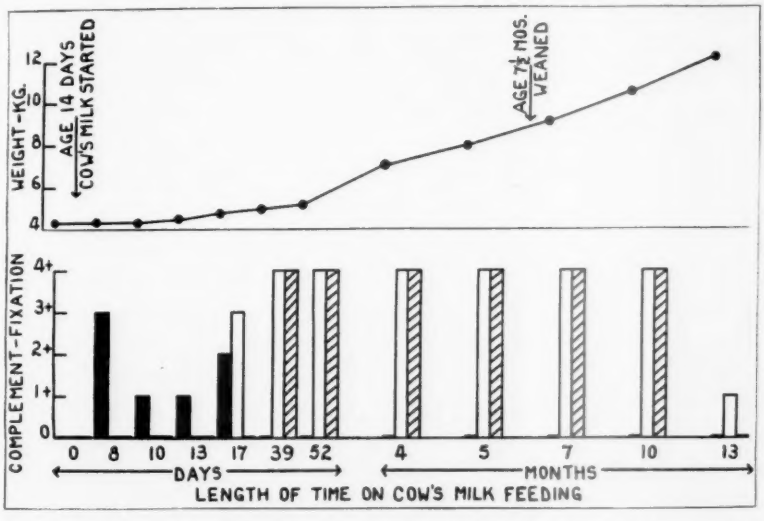

Fig. 4 (case 1).—A normal infant, who weighed 4,360 Gm. at birth, was given a complementary formula of boiled cow's milk 165 cc., water 60 cc. and cane sugar 12 Gm. on the fourteenth day. The same type of formula was gradually increased in amount until the infant was weaned at 7½ months. Accessory and supplementary foods were added to the diet at the usual ages.

In this and the following chart the black columns represent milk antigen; the white columns, skimmed milk antibodies, and the cross-hatched columns, lactalbumin antibodies.

the antigen nor the antibody of cow's milk has been detected in any one of a group of 22 persons over 5 years of age.

The brief histories of 2 infants are given as being typical of a number of those followed up with repeated examinations over a period of about a year.

Charts 4 (case 1) and 5 (case 2) illustrate the absorption of cow's milk protein with considerable regularity during the first few weeks of

artificial feeding, the development of specific antibodies, the occasional absorption of small amounts of antigen after the antibodies were formed and the final disappearance of antibodies about one year later.

COMMENT

The results of this investigation definitely confirm the previously advanced hypothesis, i. e., that following the initial ingestion of a protein food, such as cow's milk, which is an ordinary component of the infant's diet and is fed in customary amounts, an appreciable amount of incompletely digested protein is absorbed and is demonstrable in the circulating blood.

Detected much more frequently during the first few days after its introduction, this antigen continues to enter the blood stream in small

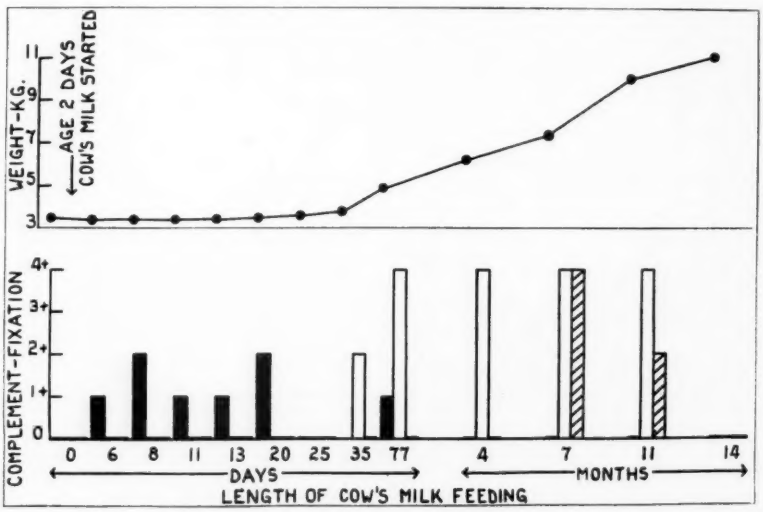

Fig. 5 (case 2).—A normal infant was delivered by cesarean section and weighed 3,540 Gm. at birth. Because of the condition of the mother the infant was never breast fed. A formula of boiled cow's milk 225 cc., water 75 cc. and cane sugar 15 Gm., was started on the second day, and the same type of formula was gradually increased. Accessory and supplementary foods were added to the diet at the usual ages.

quantities for several months, even after antibodies are present in considerable strength. As pointed out by Opie,[21] this apparent discrepancy is probably due to the multiplicity of antigens introduced in cow's milk, and lactalbumin, for instance, may be found to coexist with the antibody for casein.

21. Opie, E. L.: The Relation of Antigen to Antibody (Precipitin) in the Circulating Blood, J. Immunol. **8**:55, 1923.

The results of this investigation are essentially in agreement with those of Anderson, Schloss and Myers,[15] who used the precipitin test. They observed that the specific precipitins disappeared from the circulating blood within a few weeks. The complement-fixation antibody, as determined in this study, however, may remain as long as two years. This is probably due to a difference in the sensitivity of the two methods. The complement-fixation antibody is either more readily detected in great dilution or persists for a longer period than do the precipitins.

In most previous investigations the precipitin test has been employed, and the question of specificity of the complement-fixation test naturally arises. Definite evidence supporting the specificity of this method is the absence of a positive reaction for either lactalbumin or cow's milk antibody in any nursing infant who had never received cow's milk. This held true in all infants, irrespective of age, and depended solely on the time of institution of artificial feeding. The results applied to infants who were entirely breast fed for six months as well as to those whose artificial feedings were instituted during the first few days of life.

The mechanism whereby the body is protected from the continued absorption of appreciable amounts of foreign protein remains a mystery. Three possibilities naturally arise: first, that by some means the gastro-intestinal wall becomes impermeable to each newly introduced protein after it has been ingested for a certain length of time; second, that there is an alteration in the digestive enzymes so that they finally become capable of producing complete denaturization, and, third, that even though foreign protein is absorbed as such, it may be neutralized by some hitherto unrecognized immune reaction. The present study suggests that at least for a period of several months the gastro-intestinal wall remains permeable to minute quantities of milk protein.

It has been suggested that there may be transmission of either foreign protein or antibodies through mother's milk. The observations of Donnally [22] and György [23] showed that minute amounts of egg protein may be detected in the milk of lactating women following the ingestion of raw egg white. From this it has been inferred that such ingestion of foreign protein may lead to an immunologic response in the nursing infant. Our investigation offers no data bearing on the ingestion of breast milk containing egg, but the fact that no trace of either cow's milk protein or cow's milk antibody was detected in the blood of infants entirely breast fed for several months would seem

22. Donnally, H. H.: The Question of the Elimination of Foreign Protein (Egg-White) in Woman's Milk, J. Immunol. **19**:15, 1930.

23. György, P.: Eiklar-Antigen in der Frauenmilch, Jahrb. f. Kinderh. **132**:1, 1931.

to indicate that significant amounts of cow's milk protein were not present in the breast milk.

In addition to their interest from the standpoint of physiology, the value of immunologic studies in infants should lie in the advancement of the knowledge concerning the development of hypersensitivity. It has been observed by Rackemann [24] and others that children frequently manifest the first symptoms of hypersensitivity to antigenic substances a few days or weeks after initial exposure. This interval coincides with that which precedes the development of the antibodies observed in this investigation. In the average infant this process is passed over without incident. In the infant with the inherited tendency for hypersensitivity, however, it is conceivable that this mechanism may be altered so that the clinical manifestations of allergy result. There is at present, however, no available information to support this hypothesis.

The presence of complement fixation antibody for cow's milk was recently detected in the blood of 40 of 69 healthy, artificially fed infants by György, Moro and Witebsky.[25] In none of these infants could either passive transfer or cutaneous reactions be demonstrated. Using a similar technic, Strobl and Wasitzky [26] noted complement-fixation antibodies for egg albumin and cow's milk in a large number of infants, children and adults tested. These authors also reported the presence of complement-fixation antibodies, detectable only when high dilutions of antigen were used, in the blood of infants with eczema.[27]

In conclusion, the real significance of this investigation lies in the demonstration of a physiologic phenomenon, characterized by the temporary absorption of food protein after its initial introduction in ordinary quantities into the diet of the normal infant.

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24. Rackemann, F. M.: Can Hypersensitiveness Be Acquired? J. A. M. A. **84**:489 (Feb. 14) 1925. Simon, F. A., and Rackemann, F. M.: The Development of Hypersensitiveness in Man, J. Allergy **5**:439, 1934.

25. György, P.; Moro, E., and Witebsky, E.: Milchantikörper im Serum von Säuglingen, Klin. Wchnschr. **10**:821, 1931.

26. Strobl, A., and Wasitzky, A.: Ueber das Vorkommen von komplementbindenden Ei- und Milchantikörpern im Blutserum, Monatschr. f. Kinderh. **52**:95, 1932.

27. György, P.; Moro, E., and Witebsky, E.: Eiklarempfindlichkeit bei Eczema infantum, Klin. Wchnschr. **9**:1012, 1930; Weitere Beobachtungen über trophallergische Hautempfindlichkeit im frühen Kindesalter, ibid., p. 1435; Weitere Erfahrungen über Trophallergie beim Eczema infantum, ibid. **11**:1172, 1932. Strobl, A., and Wasitzky, A.: Untersuchungen über die alimentäre Allergie des Ekzemkindes, Monatschr. f. Kinderh. **54**:53, 1932.

MENTAL DETERIORATION ASSOCIATED WITH CONVULSIONS AND HYPOGLYCEMIA

REPORT OF TWO CASES

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The discovery of hypoglycemic shock which follows the removal of the liver and overdosage with insulin has led to reports of a number of cases of convulsions in children associated with a low concentration of the blood sugar. Undoubted cases of convulsions due to a low concentration of blood sugar have been associated with tumors of the islets of Langerhans. The following cases are of interest in that they show how difficult the interpretation of a low blood content associated with convulsions may be.

REPORT OF CASES

CASE 1.—Mary A., was born in the obstetric service of the New Haven Hospital on March 3, 1927, after an estimated gestation of seven months. The weight at birth was 1,190 Gm.; the length, 37 cm., and the circumference of the head, 28 cm. The mother was treated in the obstetric ward for toxemia of pregnancy, with vomiting, hypertension and albuminuria. Labor was induced by a bougie; the baby was born by a rather precipitate breech delivery. The infant breathed spontaneously and under care of the pediatric service apparently grew unusually well. On June 6 she was discharged, at the age of 94 days, weighing 3,200 Gm. and measuring 49 cm. in length and 33.5 cm. in the circumference of the head. On July 18 in the dispensary she was noted to be spastic but otherwise apparently normal. Her teeth erupted at 7 months, and she walked at 2 years. She never learned to talk and was obviously mentally retarded.

On May 31, 1930, at the age of 38 months, she was taken to the dispensary because she acted queerly early in the morning, vomited and was difficult to control. The mother said the child acted as though she were going to have a convulsion. She was sent home but returned a few hours later because she had had a convulsion at noon. Physical examination revealed mild rhinopharyngitis, with the temperature 38.5 C. (101.3 F.). The child's temperature was never elevated after the first day, and she was discharged after a week in the hospital. The child was obviously mentally deficient, but the results of the neurologic examination were negative at this time. Subsequently the patient was readmitted to the hospital six times for convulsions, the admissions occuring at the ages of 38, 43, 47, 52, 58 and 66 months. The cause of each admission was a convulsion lasting from five to ten minutes and usually occurring between 4 and 5 a. m., though the first two took place in the evening. In two instances a convulsion

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occurred at 4 a. m. and was repeated about three hours later. In some attacks the convulsion was almost entirely on the left side and was succeeded by a transient, flaccid paresis of the face, arm and leg on the left side. Only once did a convulsion occur when the child was not brought to the hospital.

When the child was 39 months old, a psychometric examination by Dr. M. Putnam showed her to have a mental development of about 60 per cent of the normal. At this time the spinal fluid revealed no abnormality. When she was 43 months old a roentgenographic examination of the skull after injection of air into the cerebrospinal spaces showed normal ventricles and cortical markings.

After the convulsion at the age of 47 months, the sugar content of the blood (Folin-Wu) [1] was 31 mg. per hundred cubic centimeters. In spite of the intravenous infusion of 140 cc. of a 10 per cent solution of dextrose at this time, the child remained comatose for several hours. At 47 months, the sugar content of the blood and spinal fluid (Somogyi) shortly after admission because of a matutinal convulsion was too low to be determined (less than 20 mg). Intravenous infusion of dextrose seemed to bring the child out of the coma immediately at this time. At the age of 57 months the blood sugar content (Somogyi) was 67 mg. shortly after a convulsion. No more determinations of blood sugar were made shortly after convulsions. The following figures show the tolerance to intravenous injections of dextrose (0.33 Gm. of dextrose per kilogram in a 50 per cent solution, administered after a fast of eighteen hours; Folin-Wu method) when the child was 58 months old and weighed 13.5 Kg.

Time After Fasting, Minutes	Sugar of Capillary Blood, Mg. per 100 Cc.	Time, Minutes	Sugar of Venous Blood Mg. per 100 Cc.
0	70		
6	201	8	177
20	146	22	140
38	112	40	95
82	60	85	80

Four days later, the injection of 0.5 cc. of 1:1,000 solution of epinephrine (after a fast of eighteen hours) gave the following results (Folin-Wu method):

Time After Fasting, Minutes	Sugar of Capillary Blood, Mg. per 100 Cc.	Time, Minutes	Sugar of Venous Blood Mg. per 100 Cc.
0	79	0	67
60	120		
90	141	90	134

During the final admission the cerebrospinal fluid was normal. The results of roentgenographic examination of the skull after injection of air were interpreted as follows: "Encephalography demonstrated well filled lateral and third ventricles,

1. Determinations of blood sugar were made by the Shaffer-Hartmann titration methods (Peters, J. P., and Van Slyke, D. D.: Methods, in Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, vol. 2, p. 465).

As indicated in the text, the titration was run on the filtrate from a Folin-Wu or Somogyi precipitation of proteins. The Somogyi filtrate gives results lower by about 27 mg. than the Folin-Wu filtrate.

which appeared to be slightly enlarged. There was a decrease in the cortical markings of the right frontal and parietal regions as compared to the left." At this time the head measured 49.5 cm. and the chest 53 cm., and the height was 110 cm. The child was sent to the Connecticut Training School for the Feeble Minded and Epileptic. Wassermann tests of the blood and spinal fluid repeatedly gave negative results.

In summary a patient with mental deficiency and lesion of the cerebral cortex demonstrable by encephalographic examination showed repeated convulsions. Some of the convulsions were associated with a minimal concentration of blood sugar but others with a normal concentration. The lack of prompt response to intravenous injection of dextrose indicated that the hypoglycemia was probably not the cause of the convulsion.

CASE 2.—John B. was the first-born child of normal parents. The full term delivery took place at home; the weight at birth was "9 pounds" (4,080 Gm.). Three days after birth a convulsion occurred. The patient was seen in the ophhtalmologic clinic at 10 months of age, because of strabismus and because the mother felt he could not see. At this time the visual defect was interpreted as probably due to defective mental development. Mild diarrhea accompanied by a convulsion occurred when the child was 17 months old.

The patient was first seen by the pediatric service at 29 months of age. The day before admission to the hospital he vomited in the morning and ate very little that day. The day of admission he was found stiff on waking at 8 a. m., and fifteen minutes later he had a generalized convulsion followed by a period of drowsiness lasting about two hours. The child was fairly well developed but thin. The reflexes were active and equal, and no loss of muscular power or sensation was made out. On standing or walking the patient presented a peculiar ataxia, which suggested a cerebellar disorder. There was external squint with deviation of the visual axis to the left. The child was considered to show the mental development of a low grade idiot. The cerebrospinal fluid was normal. The Wassermann reaction of the blood and spinal fluid was negative. One week later the child was admitted because of another convulsion preceded by a similar period of vomiting and fasting. On admission the following concentrations in the serum were found: bicarbonate, 22.7; chlorine, 95.8, and total base, 148.4, milliequivalents per liter, and protein, 6.43 per cent. Except for the low chloride content, which may be explained by the vomiting, the findings were normal. At this time the skull plate revealed no abnormalities and the sella turcica was normal. The boy was readmitted to the hospital eleven times up to the age of 65 months with similar complaints and findings. During the past year he was treated nine times in the accident service for convulsions and had numerous convulsions when he was not seen by a physician.

When he was 31 months old, the amount of sugar on a Folin-Wu precipitate was found to be 31 mg. per hundred cubic centimeters of blood, while the boy was still stuporous after a convulsion. A few days later the effects of an eighteen hour fast were investigated. Four hours after the last meal the blood sugar (Folin-Wu) was 99 mg. per hundred cubic centimeters, and after eighteen hours of fasting, 35 mg. At this time the serum showed: bicarbonate, 17.8; chlorine, 102.6; acetone, 3.9, and total base, 145, milliequivalents per liter, and protein, 7.1 per cent. The urine was examined as voided and gave a positive reaction to the nitroprusside test for acetone after twelve hours of fasting. During the fast the child became a little more stuporous than normal but did not have a convulsion. At 47 months the presence of blood sugar could not be detected on a Somogyi

precipitate shortly after a convulsion. After the intravenous injection of 0.33 mg. of dextrose per kilogram of body weight, the following values were found for blood sugar (after a fast of twelve hours; Folin-Wu precipitate):

Time After fasting, Minutes	Capillary Blood Mg. per 100 Cc.	Venous Blood Mg. per 100 Cc.
0	72	72
5	232	216
20	154	164
40	96	92
80	104	110

A few days later the reaction to 0.5 cc. of a 1:1,000 solution of epinephrine was as follows:

Period of Fasting, Hours	Venous Blood, Mg. per 100 Cc.
4	99
18	34
22 (1½ hours after epinephrine)	27

During this experiment, electrolyte studies revealed that ketone bodies had accumulated to a concentration of 2.5 milliequivalents per liter, while the amount of bicarbonate decreased from 23.7 to 20.3 milliequivalents per liter in the serum. The concentrations of chloride and total base showed no significant variation.

At 40 months, blood sugar (Somogyi) was again absent shortly after a convulsion. However, at 46 months the concentration (Somogyi) was 204 mg. per hundred cubic centimeters while the patient was still stuporous after a convulsion. The concentrations of serum electrolytes (bicarbonate, chloride, protein, acetone, phosphate, sodium, potassium and calcium) were normal at this time. Shortly thereafter the boy fasted for eighteen hours and the reaction to 5 units of insulin was investigated. The blood sugar content after the fast (Somogyi) was less than 20 mg. One, two and four hours after the injection of insulin, the concentration remained low (less than 20 mg.). No reaction occurred at this time. The blood sugar content (Somogyi) after a convulsion when the child was 47 and 53 months was 180 and 86 mg., respectively.

At 31 months the results of a roentgen examination of the skull after injection of air were interpreted as follows: "There was no definite abnormality in either lateral ventricle. The third ventricle was only faintly visualized and appeared normal in size, and there was a shadow in the region of the fourth ventricle which was thought to be due to a small amount of air. There was a small amount of air in the cisterna. With change in position of the patient, a small amount of air was noted over the cerebral cortex on the right side. The air was movable from the anterior to the posterior region of the cortex and was definitely limited to the right side. The cortical air markings noted appeared normal. The collection of air over the cortex on the right side, which shifted with change in position of the patient was considered pathologic, possibly due to an old cortical injury."

The boy was treated by intravenous injection of a 10 per cent solution of dextrose, and at first this treatment seemed to be effective. However, usually the child remained stuporous for some time after injections of dextrose. Later the convulsions were obviously not affected by the injections of dextrose. In any

case the effect of dextrose was never as striking as that seen in the cases of hypoglycemic convulsions which are associated with tumor of the pancreatic islets or occur after an overdose of insulin.

In summary, a patient with mental deficiency and lesions of the cerebral cortex demonstrable by encephalographic examination showed repeated convulsions. Some of the convulsions were associated with a minimal concentration of blood sugar, but some were associated with normal values. Although eighteen hours of starvation induced an unusually low concentration of blood sugar, no convulsions were induced by this procedure. When starvation induced the low blood sugar content, the lack of increase following injection of epinephrine suggests that the glycogen reserves were quickly exhausted. Since the injection of insulin did not induce hypoglycemic symptoms in spite of the low blood sugar content, the disturbance in carbohydrate metabolism is probably not due to hyperinsulinism.

COMMENT

The association of hypoglycemia with convulsions is definite after the removal of the liver [2] and an overdose of insulin and in cases of hyperinsulinism [3] associated with tumors of the pancreatic islands and perhaps with hypertrophy of the islands.[4] In addition, convulsions in children are occasionally associated with low values for blood sugar.[5] However, children frequently have convulsions, especially when the temperature rises sharply and suddenly, and in most of these cases hypoglycemia is not found. Furthermore, in the cases with the most persistent convulsions the condition is associated with organic disease of the brain, which is obvious in cases of epilepsy with mental deterioration and jacksonian epilepsy but is only suggested by analogy in idiopathic epilepsy.

During the past several years a number of specimens of blood from children entering the New Haven Hospital during or soon after a convulsion were analyzed for blood sugar. Of these, thirteen showed from 85 to 110 mg. of sugar in the blood; three, from 110 to 125 mg.,

2. Mann, F. C., and Magath, T. B.: Studies in the Physiology of the Liver: II. The Effect of the Removal of the Liver on the Blood Sugar Level, Arch. Int. Med. **30**:73 (July) 1922.

3. Bibliographies are given in the following articles: Bowen, B. R., and Beck, G.: Insulin Hypoglycemia, Ann. Int. Med. **6**:1412, 1933. Gammon, G. D., and Tenery, W. C.: Hypoglycemia: The Clinical Syndrome, Etiology and Treatment, Arch. Int. Med. **47**:829 (June) 1931.

4. Finney, J. M. T., and Finney, J. M. T., Jr.: Resection of the Pancreas, Ann. Surg. **88**:584, 1928.

5. (*a*) Ross, S. G., and Josephs, H.: Observations on the Metabolism of Recurrent Vomiting, Am. J. Dis. Child. **28**:447 (Oct.) 1924. (*b*) Josephs, H.: Fasting as a Cause of Convulsions, ibid. **31**:169 (Feb.) 1926; Recurrent Vomiting, ibid. **31**:657 (May) 1926. (*c*) Griffith, J. P. C.: Hypoglycemia and the Convulsions of Early Life, J. A. M. A., **93**:1526 (Nov. 16) 1929. (*d*) Elias, H. L., and Turner, R.: Spontaneous Hypoglycemic Shock in Children: Report of Four Cases, ibid. **98**:2198 (June 18) 1932.

and five, from 60 to 70 mg. Apparently hypoglycemia does not occur commonly in cases of convulsions in childhood.

Although the extremely low values for blood sugar found in the two cases described suggest that the convulsions could be precipitated by the hypoglycemia, close examination shows that this was probably not the case. The history of matutinal convulsion is suggestive of hypoglycemia at the time of the convulsions in both cases. However, in each case, convulsions occurred with normal or high values for blood sugar. In case 2, a low value could be produced by starvation without inducing a convulsion. Furthermore, the intravenous injection of dextrose did not produce the prompt alleviation of symptoms which occurs in the cases of convulsions clearly produced by hypoglycemia, such as those associated with hepatectomy,[2] an overdose of insulin or hyperinsulinism.[3] Furthermore, the finding of hypoglycemia after a convulsion may be the result rather than the cause of the convulsion.

I have been unable to find precisely analogous cases in the literature. Low values for blood sugar associated with convulsions in children have been reported by Ross and Josephs,[5a] Josephs,[5b] Elias and Turner [5d] and Griffith.[5c] The fifth case observed by Griffith is probably more nearly the same as the cases herein described, since the patient had epilepsy owing to injury to the head and failed to respond to dextrose.

Numerous reports of hypoglycemic shock and convulsions in adults have been reported in association with tumors of the pancreatic islands and perhaps with hyperplasia of the islands.[6] In these cases, increased susceptibility to insulin could be demonstrated, and the response to dextrose was the same as the response to dextrose after an overdose of insulin. In case 2 increased susceptibility to insulin shock was not demonstrated, though the low blood sugar content at the time of the test may have made the experiment unsatisfactory. However, in case 2 the failure to show an increase in blood sugar after injection of epinephrine is not in favor of the idea that the hypoglycemia is due to hyperinsulinism. The lack of response to epinephrine is difficult to explain but may be due to exhaustion of hepatic glycogen.

With necrosis of a large part of the liver in acute yellow atrophy from poisoning with phosphorus, chloroform, phenylhydrazine, etc., and in diphtheria, hypoglycemia due to failure of glyconeogenesis may be

6. Footnotes 3 and 4. Graham and Hartman (Graham, E. A., and Hartman, A. F.: Surg., Gynec. & Obst. **59**:474, 1934) reported a case in which a child 1 year of age had frequent convulsions and hypoglycemia. The child showed marked deficiency in mental development. Removal of about seven-eighths of the pancreas was followed by disappearance of convulsions and hypoglycemia. Although the child appeared brighter, psychometric examination showed only questionable improvement after nine months. This case seems to be analogous to those reported.

found. Since extensive hepatic involvement is necessary to produce hypoglycemia by failure of glyconeogenesis, such a mechanism may be excluded in the cases reported in this paper.

Hypoglycemia and hypoglycemic symptoms are ascribed to failure of glycogenolysis in Gierke's disease. The absence of enlargement of the liver probably excludes this mechanism in the present cases.

The patients, by exclusion, seemed to exhibit a disturbance in the hormonal or nervous control of the blood sugar. Macleod [7] stated that a region in the pons can control the level of the blood sugar through nervous control over the adrenals and pancreatic islands. Cushing [8] pointed out evidence of nervous control of the blood sugar which in part may work through activating the hypothesis. The work of Housay and Biasotti [9] particularly called attention to the importance of the hypophysis in sugar metabolism. Wilder [10] described two cases of hypoglycemia in adults associated with signs and symptoms of hypophyseal dysfunction. While the mechanism of the nervous (or neurohypophyseal) control of the blood sugar is not understood, considerable evidence of such a control exists. Since in the present cases there was no evidence of disturbance of growth or of other hypophyseal dysfunction but gross lesions of the brain were seen in the roentgenograms, it is possible that a disturbance of the nervous control of the blood sugar was the cause of the failure in the regulation of the blood sugar.

Grayzel [11] demonstrated degenerative changes in the cortical cells of rabbits subjected to repeated convulsions by injection of insulin. It does not seem probable that the cerebral degeneration in these cases was the result of repeated attacks of hypoglycemic convulsions.

Since these patients were of such low mentality, it is difficult to exclude the minor symptoms of hypoglycemia. Sweating and shock were absent when the concentration of blood sugar was too low to be determined on a Somogyi precipitate by the Shaffer-Hartmann method. During the periods of hypoglycemia produced by starvation, some weakness was exhibited but probably not beyond that often seen after a prolonged fast. Certainly extremely low values for blood sugar did not always induce convulsions; intravenous injections of dextrose did

7. Macleod, J. J. R.: The Control of Carbohydrate Metabolism, Lancet **1**:1079, 1932.

8. Cushing, H.: Neurohypophyseal Mechanisms from the Clinical Standpoint, Lancet **2**:119 and 175, 1930.

9. Housay, B. A., and Biasotti, A.: The Hypophysis, Carbohydrate Metabolism and Diabetes, Endocrinology **15**:511, 1931.

10. Wilder, J.: Ein neues hypophysäres Krankheitsbild: Die hypophysäre Spontanhypoglykämie, Deutsche Ztschr. f. Nervenh. **112**:192, 1930.

11. Grayzel, D. M.: Changes in the Central Nervous System Resulting from Convulsions Due to Hyperinsulinism, Arch. Int. Med. **54**:695 (Oct.) 1934.

not dramatically relieve convulsions associated with marked hypoglycemia, and some convulsions occurred when a normal blood sugar content was demonstrated. The patients seem to have had disease of the brain causing convulsions and a disturbance in the regulation of the blood sugar, and the nervous symptoms should be related to the lesions in the brain rather than to the hypoglycemia.

SUMMARY

Two cases of convulsions in children with mental deficiency and roentgenologic evidence of anatomic changes in the brain are reported. Hypoglycemia occurred in both cases shortly after some convulsions but not after all. Hypoglycemia (sugar content below 20 mg. per hundred cubic centimeters) could be produced by starvation in one case without inducing a convulsion. It is suggested that the disturbance in the regulation of blood sugar may be due to lesions of the brain.

CHANGES IN THE RATE OF THE HUMAN FETAL HEART IN RESPONSE TO VIBRATORY STIMULI

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That the human fetus is capable of perceiving sound vibrations and of responding to them by movements of the extremities has previously been reported. Forbes and Forbes [1] reported the case of a woman who while attending musical concerts felt a great deal of fetal movement whenever the audience applauded. Peiper [2] reported an increase of fetal activity immediately following certain sound stimuli. Ray,[3] in an attempt to condition the human fetus, elicited a movement response to the sound of two boards clapping together. We [4] reported the movement response of the fetus to sound by months during the last three months of intra-uterine life. We [5] demonstrated the existence of this response at an earlier age than it had generally been assumed to be present. Minkowski [6] and others have demonstrated on premature human fetuses from interrupted pregnancies the presence of a tactile sense and a response to tactile stimuli before the third month. Angulo y González,[7] Swenson,[8] Windle and Griffin [9] and others have reported the muscular response to tactile stimuli in animal fetuses.

From the Samuel S. Fels Fund.

1. Forbes, H. S., and Forbes, H. B.: Fetal Sense Reactions: Hearing, J. Comp. Psychol. **7**:353, 1927.

2. Peiper, A.: Sinnesempfindungen des Kindes vor seiner Geburt, Monatschr. f. Kinderh. **29**:236, 1925.

3. Ray, Wilbert: A Preliminary Report of a Study of Fetal Conditioning, Child Development **3**:175, 1932.

4. Sontag, L. W., and Wallace, R. F.: A Preliminary Report of the Fels Fund: Study of Fetal Activity, Am. J. Dis. Child. **48**:1050 (Nov.) 1934.

5. Sontag, L. W., and Wallace, R. F.: The Movement Response of the Human Fetus to Sound Stimuli, Child Development **6**:4, 1935.

6. Minkowski, M.: Sur les mouvements, les réflexes et les réactions musculaires du foetus humain de 2 à 5 mois et leur rélations avec les système nerveux foetal, Rev. neurol. **37**:1105 and 1235, 1921.

7. Angulo y González, A. W.: Neurological Interpretation of Fetal Behavior: The Progressive Increase of Muscular Activity in Albino Rat Fetuses, Anat. Rec. **42**:17, 1929.

8. Swenson, E. A.: The Development of Movement of the Albino Rat Before Birth, Thesis, University of Kansas, 1926.

9. Windle, W. F., and Griffin, A. M.: Observations on Embryonic and Fetal Movements of the Cat Fetus, J. Comp. Neurol. **52**:149, 1931.

During the period of accumulation of data for a previous report on the muscular response to vibratory stimuli of human fetuses, it occurred to us that the muscular response was of such magnitude that it might produce an increase in the rate of the fetal heart as a compensatory action to the muscular fatigue of the fetus. In order to check this theory, the fetal heart rate was counted during the taking of the records of fetal movement.

METHOD OF TAKING AND RECORDING FETAL HEART RATE

Our observations were made by means of a stop-watch and stethoscope placed on the abdomen of the mother at the point where the fetal heart sound could be heard most clearly. In place of counting the number of beats heard during a given length of time, as is commonly done, we measured the time which elapsed during the counting of 10 beats. A table was then constructed by which the elapsed time for 10 beats could instantly be converted into the rate per minute of the fetal heart. The count was as follows: As soon as a few beats had been heard to establish the rhythm, the stop-watch was snapped on at the point of maximum intensity of a fetal heart sound. As the watch was snapped on, the count was started, as 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, ending at the point of maximum intensity of the sound on which the count of 10 was made. An assistant was employed at all times to record the results of the determinations.

We feel that the method is subject to considerably less error than is the fractional minute method, in which there is error from the confusion of fractional beats which sometimes must be dealt with when counting heart beats for a given length of time. Since only 10 beats are counted by our method, any interference with the perception of the fetal heart, such as uterine souffle or movement of gas in the intestine, can eliminate only a very short period of the record. By the use of the 10 beat method, the inaccuracies resulting from fatigue and confusion when counting the pulsations of a rapidly beating fetal heart for a minute or half a minute are eliminated.

The accuracy of the investigator who made the determinations of fetal heart rate was checked by having him count and time in a similar manner clicks of a known frequency (from 120 to 180 beats per minute) which were sent through an ordinary telephone headset. During several hundred of these checks, the time recorded for ten of these clicks did not vary more than one-tenth second from the actual elapsed time of 10 clicks. A second check was made by having two persons record the rate of the same fetal heart at the same time. It was found that the difference between the results of the two investigators was never more than one-tenth second. The limit of accuracy of any individual record was therefore from 1 to 3 beats, according to the rate of the heart. With from six to nine samples being taken per minute, the errors tend to become compensated, and the accuracy of the average rate per minute is much higher than that of any individual sample.

The period of pregnancy during which observations were made ranged from one hundred and twenty-seven days before birth to one day before birth. The observations are designated as so many days prenatal, or before birth, because of the absence of any accurate means of determining fetal age. The duration of the pregnancies ranged from two hundred and fifty-five days to two hundred and eighty-eight days from the beginning of the last menstruation. The infants

ranged from 2,387 Gm. to 3,454 Gm. in weight at birth. All were fully matured as far as could be determined by examination. Eight patients were used for the experiment, and a total of two hundred and seventeen records was made.

The results of these observations are shown in table 1. The mean of all the responses is shown graphically in figure 1.

From four to ten samples were recorded in each minute. A five minute control period preceded the application of the vibratory sound stimuli. Samples of fetal heart rate were taken for from five to twenty-five minutes following application of stimuli. Fetal movements, as indicated by the patient by the lighting of a

TABLE 1.—*Mean Change in Fetal Heart Rate in Response to Stimulation, by Weeks and Months Before Birth*

Prenatal Age		Patients								
Month	Week	A	B	C	D	E	F	G	H	Mean
	1	16.5	....	....	....	7.7	12.1	22.5	....	16.6
	2	12.6	....	....	....	5.0	8.1	20.2	....	13.3
	3	....	16.0	....	9.1	11.6	11.4	22.6	....	13.7
	4	....	....	28.3	14.8	−4.0	19.3	....	8.5	12.1
1		14.4	16.0	28.3	12.5	5.2	12.5	21.5	8.5	14.3±0.74
	5	....	8.5	....	14.2	14.2	17.5	15.5	50.3	16.7
	6	....	7.1	....	....	10.9	11.0	....	....	10.7
	7	....	11.2	....	....	4.0	15.1	....	....	13.0
	8	....	15.1	21.4	7.7	3.5	16.7	....	....	12.9
2			11.5	21.4	13.1	7.5	13.9	15.5	50.3	13.4±0.82
	9	....	14.4	12.0	....	8.5	7.2	....	....	10.1
	10	....	9.2	14.3	2.7	7.7	2.6	....	....	8.0
	11	....	3.7	....	....	7.3	6.3	....	....	6.2
	12	....	11.3	....	....	0.9	....	....	....	5.1
3			9.0	13.1	2.7	6.8	5.1			7.8±0.83
	13	....	−6.5	....	....	7.3	3.5	....	....	1.1
	14	....	−8.7	3.6	....	....	−7.3	....	....	−2.3
	15	....	....	2.9	....	4.3	....	....	....	3.3
	16	....	....	....	....	....	....	....	....	....
4			−7.5	3.2		6.3	−1.9			0.3±0.17
	17	....	....	1.3	....	....	....	....	....	1.3
	18	....	....	0.7	....	−0.3	....	....	....	0.4
	19	....	....	....	....	−4.0	....	....	....	−4.0
	20	....	....	....	....	....	....	....	....	....
5				1.0		−2.1				−0.07±1.52
Mean.....		14.4± 1.21	7.3± 1.21	10.5± 1.83	12.0± 1.33	6.1± 0.70	11.3± 0.67	21.1± 1.38	29.4± 31.6	11.2±0.47
No. of records		11	23	23	12	56	59	31	2	217

small incandescent bulb, were recorded throughout both the control period and the period following stimulation. The button switch by which the mother was able to light the bulb remained in her hand throughout and to activate it required almost no effort.

OBSERVATIONS

In the last four weeks before birth there was a mean increase in heart rate of 14.3 ± 0.74 beats per minute; in the second month before birth, an increase of 13.4 ± 0.82 beats per minute; in the third month before birth, an increase of 7.8 ± 0.83 beats per minute; in the fourth and fifth months before birth, respectively, an unreliable decrease of

0.07 ± 1.52 beats per minute. Since in the last three months before birth there was such a marked increase in fetal heart rate following the application of vibratory stimuli, the question arises as to whether this increase is actually the result of the muscular activity of the fetus or whether it is an independent phenomenon. A study of the records obtained has convinced us that the increase is not caused entirely by an increased activity of the fetal muscles but is due in part, at least, to an

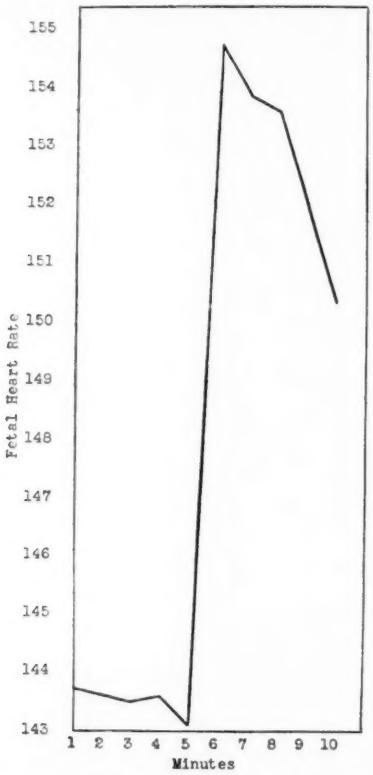

Fig. 1.—Fetal heart rate during vibratory stimulation (five minutes before and five minutes after stimulation). Two hundred and seventeen records on eight subjects were made from one to one hundred and twenty-seven days, or an average of forty days, before the birth of the infant. The number 5 indicates the point at which stimulation was begun.

entirely separate visceral response to the vibratory stimuli. Figure 2 demonstrates very well the unitary character of this response and its independence of muscular response to the stimulus. The points on the upper line represent the fetal heart rate in the first minutes following stimulation, while the points on the lower line represent the fetal heart rate during control periods in which like numbers of fetal movements

occurred. It is evident from this chart that in the control periods in which a given number of movements occurred the fetal heart rate was from 4.5 to 9 beats per minute slower than in the first minutes following stimulation in which a like number of movements occurred.

Further proof of the independence of the cardiac response from the muscular response is available from an examination of table 2. Of the seven patients on whom two hundred and fifteen experiments were made, two patients, one representing twenty-three experiments and the other fifty-six experiments, show no movement response to vibratory

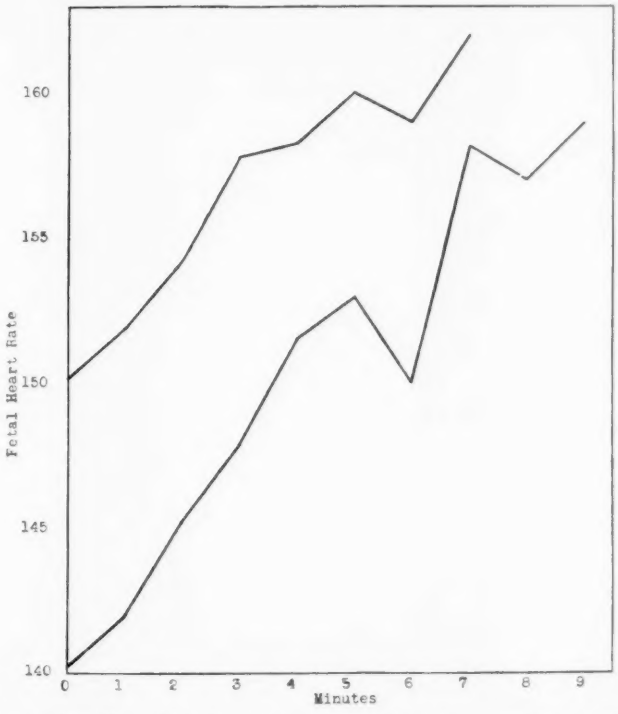

Fig. 2.—Relationship between the number of movements per minute and the mean fetal heart rate in control periods and the minute following application of stimulus. The upper line represents the fetal heart rate plotted according to the moves per minute following stimulation, while the bottom line indicates the fetal heart rate existing when the number of moves per minute was the same, but when no stimulation had been applied.

stimulation. Both show a slight but unreliable negative response. Patient B shows a very slight increase in the percentage of time the fetus was active after stimulation, while patient E shows a negative response in this respect. Yet both patients show a reliable increase in fetal heart rate following the stimulations which failed to produce in them an increase in fetal movement.

A total of fifty-seven cases was selected from all of the experiments in which no movement was observed in the minute following stimulation. The mean heart rate in these cases before stimulation was 144.7 ± 0.77 beats per minute. The mean heart rate after stimulation was 150.7 ± 0.88 beats per minute, leaving a difference, apparently the result of stimulation, of 6.0 ± 1.11 beats per minute, even though the amount of fetal movement was actually *less* in this minute than in the control period.

From the figures presented one must conclude, then, that there is a visceral response of the fetus to the application of vibrations of a frequency of 120 per second to the abdomen of the mother during the later part of pregnancy. Anatomic studies of the human fetus indicate that the vagus fibers to the heart do not enter the heart muscle until the last

TABLE 2.—*Number of Fetal Movements per Minute, Percentage of Time the Fetus Was Active and Fetal Heart Rate Before and After the Application of a Vibratory Stimulus to the Mother's Abdomen*

	A	B	C	D	E	F	G
Number of cases	11	23	23	12	56	59	31
Movements per minute, normal	0.72	0.83	1.20	1.67	2.13	1.17	0.70
Movements per minute after stimulation	1.90	0.61	3.09	2.58	1.84	1.85	3.42
Change	1.18	−0.22	1.89	0.91	−0.29	0.68	2.72
Normal percentage of time active	30	39	45	53	69	54	42
Percentage of time active after stimulation	70	47	83	92	68	69	100
Change, percentage	40	8	38	39	−1	15	58
Normal heart rate	138.2	142.3	150.2	145.4	150.3	139.2	136.8
Heart rate after stimulation	152.6	149.6	160.7	157.4	56.4	150.33	157.9
Change	14.4	7.3	10.5	12.0	6.1	11.13	21.1

lunar month of intra-uterine life. The phenomena we have observed cannot, therefore, be due to any inhibitory effect on the vagus center. Since there is evidence that sympathetic fibers enter the heart at about the seventh month of intra-uterine life, it may be that the onset of the cardiac response to vibratory stimulation occurs at the time that these fibers enter the cardiac muscle. One must consider the possibility of the response being a result of stimulation of some fetal endocrine gland, such as the adrenal. That the response is not due to the stimulation of the mother's adrenal glands is evident from the fact that it cannot be elicited at the time the fetal heart can first be heard.

As in the case of the response of the fetus to vibratory stimuli by muscular movements, the working out of normal standards for the time of onset of responses and the comparison of the time of development of this response by the fetus with this norm may yield a means of estimating the rate of development of and the maturity of that fetus.

SUMMARY

In a total of two hundred and seventeen experiments made between one day and one hundred and twenty-seven days before delivery on eight pregnant women, there was an average increase of 11.2 ± 0.47 beats per minute in the fetal heart rate following the application of vibratory stimuli of a frequency of 120 beats per second to the mother's abdomen.

This change in heart rate was distributed according to months as follows:

During the last month before birth, an average increase of 14.3 ± 0.74 beats per minute.

During the second month before birth, an average increase of 13.4 ± 0.82 beats per minute.

During the third month before birth, an average increase of 7.8 ± 0.83 beats per minute.

During the fourth month before birth, an unreliable increase of 0.3 ± 0.17 beats per minute.

During the fifth month before birth, an unreliable decrease of 0.07 ± 1.52 beats per minute.

This increase was greater than the increase due to fetal movement.

There were two cases, representing seventy-nine experiments, in which no movement response to the stimulus occurred but in which a reliable increase in heart rate did occur.

There is a total of fifty-seven experiments in which no movement occurred during the first minute following stimulation. The fetal heart rate underwent an average increase of 6.0 ± 1.11 beats per minute.

CONCLUSIONS

The human fetus is capable of responding to certain vibratory stimuli by an increase in heart rate. This response is independent of, although it may be augmented by, the muscular movement response of the fetus. The response develops about the beginning of the twenty-ninth week and increases by the month until birth. This response may prove of value as an index of intra-uterine development.

THE SUBSTANCES INVOLVED IN THE COAGULATION OF THE BLOOD OF THE NEW-BORN

V. PROTHROMBIN; QUANTITATIVE AND QUALITATIVE STUDIES OF PLATELETS IN THE NORMAL INFANT

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In a former report concerning the substances involved in the coagulation of the blood of the new-born,[1] the prothrombin was estimated by a comparison of the time necessary for plasma treated with sodium oxalate to clot after various amounts of calcium chloride were added, as described by Howell.[2] During the course of further experimentation in this field, we became dissatisfied with this method.

Whether the platelets alone are the source of prothrombin is still open to considerable controversy. However, as plasma from which all platelets have been removed will not clot for a great length of time and, conversely, plasma containing a high concentration of platelets coagulates rapidly, it seems fair to assume that the platelets are at least the principal source of prothrombin. For this reason the following studies were made.

METHOD

Our previously described method[3] for obtaining natural venous plasma was used. Platelet counts were made directly from natural venous plasma obtained after the centrifugation of whole blood in 1 cc. tubes, coated with paraffin, for one and one-half minutes at 5,000 revolutions per minute. Qualitative determinations of the platelets were made by estimating the coagulation time of the natural plasma, called "plasma A," platelet-free plasma, obtained by centrifugation for one

From the Department of Pediatrics, Rush Medical College, and the Presbyterian Hospital.

1. Sanford, H. N.; Gasteyer, T. A., and Wyat, Lois: The Substances Involved in the Coagulation of the Blood of the New-Born, Am. J. Dis. Child. **43**:58 (Jan.) 1932.

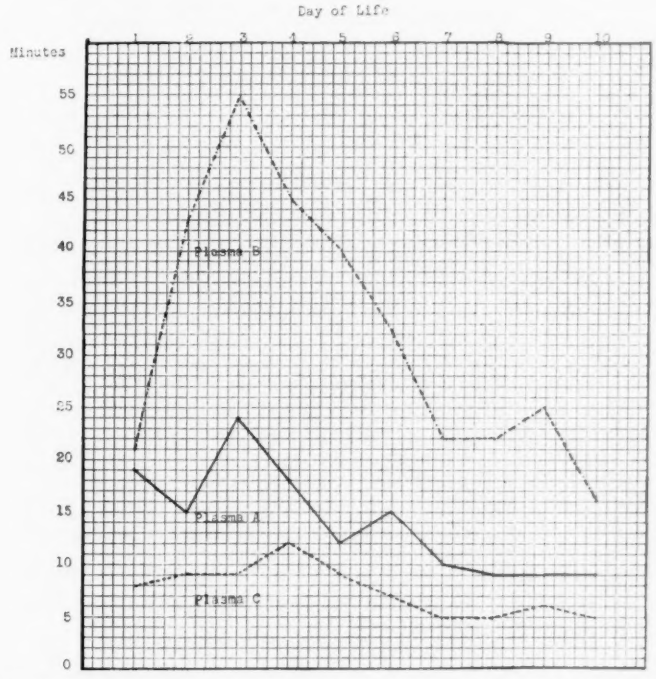
2. Howell, W. H.: Harvey Lectures, Philadelphia, J. B. Lippincott Company, 1917.

3. Leslie, E. I., and Sanford, H. N.: A Method of Qualitative and Quantitative Platelet Estimation in Their Own Plasma, J. Lab. & Clin. Med., to be published.

hour and thirty minutes, called "plasma B," and plasma containing platelet concentrate, called "plasma C."

The blood was drawn from the anterior fontanel or from the internal jugular vein; all specimens of blood containing cerebrospinal or tissue fluid were discarded.

Estimates were made on forty normal new-born infants for periods varying from twenty-four hours to ten days of life. These infants were entirely breast fed, receiving only water as a complementary feeding.



Coagulation time of fractions of plasma containing various concentrations of platelets (average for forty cases).

RESULTS

The table gives the average numbers of plasma platelets for each day of life, with the number of minutes required for coagulation of the plasma with various concentrations of platelets for each day. The chart gives these results graphically.

Daily Coagulation Time of Fractions of Plasma Containing Various Concentrations of Platelets (Average for Forty Cases)

Day of life	1	2	3	4	5	6	7	8	9	10
Number of plasma platelets	590,000	600,000	584,000	470,000	625,000	540,000	610,000	650,000	660,000	500,000
Coagulation time in minutes:										
Plasma A	19	15	24	18	12	15	10	9	9	9
Plasma B	21	43	55	45	40	32	22	22	25	16
Plasma C	8	9	9	12	9	7	5	5	6	5

COMMENT

It will be observed that the daily quantitative values for platelets in the plasma are considerably higher than those given for whole blood. As has been previously reported by us, the platelet count for the whole blood is to the platelet count of the plasma as the volume of the plasma is to the volume of the blood. This proportion should be kept in mind, as practically all determinations of platelets in the new-born have been made on whole blood. The number of platelets in the plasma sheds no particular light on the problem of coagulation. The number remains at an almost constant daily level between 500,000 and 600,000 and certainly shows no hemorrhagic tendency.

The qualitative behavior of the platelets is quite different. For natural venous plasma containing the normal number of platelets, the average coagulation time is nineteen minutes on the first day, decreases to fifteen minutes on the second, rises to twenty-four minutes on the third, falls to eighteen minutes on the fourth and to twelve minutes on the fifth, rises slightly to fifteen minutes on the sixth, then falls to ten minutes on the seventh and remains practically stationary thereafter. This increase in the coagulation time of the blood of the new-born during the first four days of life was first observed by Rhodda.[4] There has been no satisfactory explanation for this increased coagulation time before, as there is no apparent quantitative change in the platelets.

The observations made on the platelet-free plasma afford an explanation for this. The platelet-free plasma is plasma that has been shown by microscopic examination to contain no intact platelets. Changes in coagulation time for this plasma must represent prothrombin obtained by disintegration of platelets or must be a measure of the qualitative value of the platelets. On the first day of life the platelets are not abnormally resistant, and the plasma coagulates in twenty-one minutes. On the second day this resistance has increased so that disintegration has decreased, and the coagulation time increases to forty-three minutes. It increases further to fifty-five minutes on the third day, then falls to forty-five minutes on the fourth day and decreases thereafter daily as the resistance of the platelets decreases to values slightly below that present on the first day of life.

The plasma containing the platelet concentrate naturally coagulates much more rapidly than normal plasma, but even here disintegration of the platelets is delayed, increasing the coagulation time from the first day to the fourth day. The platelets then disintegrate faster, or

4. Rhodda, R. D.: A Clinical Method of Estimating the Coagulation Time of the Blood, Am. J. M. Sc. **140**:807, 1910.

rather change qualitatively, and coagulation is hastened, or the time decreases to the seventh day and remains the same thereafter.

In résumé, therefore, we may state that quantitatively there is no particular change in the platelets of the new-born for the first ten days of life. Qualitatively the platelets of the new-born show increasing resistance to disintegration until the fourth day of life, and then the resistance decreases until the tenth day, when the qualitative value of disintegration is greater than at birth.

This increased resistance to disintegration is shown by the longer time necessary for the blood to clot and explains the increase in coagulation time observed in the blood of the new-born during the first four days of life. Whether this increased resistance to disintegration is due to inherent properties of the platelets themselves or to some circulating antiprothrombin is not known, but the subject is under investigation. It appears, however, that qualitative estimations of the platelets of the blood of the new-born give a true index of the prothrombin value.

CONCLUSIONS

The number of platelets in natural venous plasma of the new-born for the first ten days of life shows practically no daily change, varying between 500,000 and 600,000.

Disintegration of platelets in the plasma of the new-born for the first ten days of life is less at birth than later, and this lack of disintegration increases until the fourth day of life. It then decreases, and by the tenth day disintegration is greater than at birth.

This resistance to disintegration of the platelets of the new-born parallels the increase in coagulation time of the blood occurring in the first four days of life.

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FURTHER STUDIES OF VIOSTEROL IN THE PROPHYLAXIS OF RICKETS IN PREMATURE INFANTS

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In a previous study [1] two of us found that a daily dose of 20 drops of a commercial preparation of viosterol 250 D (5,000 U.S.P. X units, revised 1934 [2]) was insufficient for the complete protection of premature infants from rickets. At the suggestion of Dr. Martha M. Eliot, of the Children's Bureau, Washington, D. C., we undertook the present study with another preparation of viosterol, the bio-assay of which had been made by the Food and Drug Administration, Department of Agriculture. The literature on the administration of viosterol to infants up to June 1933 was summarized in our earlier study,[1] with the exception of a paper by Barnes, Brady and James,[3] in which they compared the antirachitic effect of cod liver oil, viosterol and cod liver oil combined with viosterol. They also studied a control group of infants to whom no antirachitic therapy was given. Their observations are summarized in table 1. The maintenance of a normal level of the calcium-phosphorus product was used as the main criterion of the presence or absence of rickets. Barnes and his associates concluded that viosterol alone was a much less satisfactory agent than cod liver oil in approximately equivalent rat unit potencies. They expressed the opinion that they were not justified in considering a given number of rat units of

From the Department of Diseases of Children, College of Physicians and Surgeons, Columbia University, the Babies Hospital and the Sloane Hospital for Women.

1. Davidson, L. T., and Merritt, K. K.: Viosterol in the Prophylaxis of Rickets in Premature Infants: Clinical, Chemical and Roentgenologic Observations, Am. J. Dis. Child. **48**:281 (Aug.) 1934.

2. Throughout this paper U. S. P. unit refers to the U. S. P. X unit as revised in 1934.

3. Barnes, D. J.; Brady, M. J., and James, E. M.: The Comparative Value of Irradiated Ergosterol and Cod Liver Oil as a Prophylactic Antirachitic Agent When Given in Equivalent Dosage According to Rat Units of Vitamin D, Am. J. Dis. Child. **39**:45 (Jan.) 1930.

vitamin D in viosterol equivalent to the same number of units in cod liver oil. It seems possible that the presence of rickets in the children in their study might have been detected by roentgenograms, since it has been repeatedly shown that rickets may be observed by roentgen examination when the calcium-phosphorus product is normal.

Since June 1933, various observers have continued to emphasize the comparative ineffectiveness of viosterol as compared with other antirachitic agents, particularly cod liver oil. Alfred Hess and his co-workers were early concerned with the curative and prophylactic potency of viosterol as compared, first, with standard preparations of cod liver oil, and, later, with other forms of vitamin D, such as cod liver

TABLE 1.—*Percentage of Protection or Cure with Various Antirachitic Agents (According to Barnes, Brady and James* [3])

Agent	Daily Dosage	Unitage		Number of Cases	Percentage of Protection or Cure
		Steenbock	U.S.P.		
Cod liver oil	3 teaspoons	1,400	3,920	64	95
Viosterol	60 drops	1,250	3,500	57	44
Cod liver oil with viosterol	3 teaspoons	3,750	10,500	49	98
No therapy				46	Approximately 44

TABLE 2.—*Comparative Dosage (Rat Units) of Various Antirachitics (According to Hess)*

Agent	Minimum Protective Dosage		Unit Ratios
	Dose	Units	
Viosterol	8 drops	600	15
Cod liver oil	2 teaspoons	240	6
Milk from cows fed irradiated yeast	750 cc.	80	2
Irradiated milk	750 cc.	40	1

oil concentrate and the fortified milks, including irradiated milk and milk from cows fed irradiated yeast. In 1930 they [4] demonstrated that more rat units of viosterol than of cod liver oil were necessary to protect infants from rickets or to cure rickets in infants. In 1933 [5] they compared the curative effects of viosterol in a daily dose of 320 rat units with those of irradiated milk in a daily dose of from 30 to 40 rat units and milk from cows fed irradiated yeast in a daily dose of from 60 to 90 rat units. Irradiated milk in a dose of from 35 to 40 rat units per day was the most effective. Viosterol required the largest number of rat units. Hess again asserted that the respective biologic

4. Hess, A. F.; Lewis, J. M., and Rivken, H.: Newer Aspects of the Therapeutics of Viosterol, J. A. M. A. **94**:1885 (June 14) 1930.

5. Hess, A. F., and Lewis, J. M.: An Appraisal of Antirachitics in Terms of Rat and Clinical Units, J. A. M. A. **101**:181 (July 15) 1933.

potencies of various antirachitic agents as expressed in rat units are not interchangeable and that each must be appraised for itself clinically and then expressed in terms of rat units. In a later article Hess [6] stated that the minimum protective doses, in rat units, of viosterol, cod liver oil, milk from cows fed irradiated yeast and irradiated milk have ratios to each other of 15, 6, 2 and 1, respectively, as summarized in table 2. These ratios approximate closely those accepted at present.

Mazzeo [7] used a preparation of irradiated ergosterol, the bio-assay of which was not stated, in a series of infants with rickets. The dose was from 10 to 30 drops daily. Clinical improvement was noted in from three to five months. Normal values for serum calcium were reached or exceeded in from ten to fifteen days and those for serum phosphorus in from six to eight weeks. Roentgenographic changes were noted in from three to five months. Evaluation of such a report is difficult because of the author's failure to state the vitamin D content of the preparations used.

May and Wygant [8] studied the prophylactic use of and tolerance for haliver oil with viosterol in premature and weakling infants. The infants were given from 6 to 24 drops of a combination of viosterol 250 D and halibut liver oil of which the vitamin A potency ranged from 5 A to 60 A. The premature infants who received a dilution having a vitamin A potency which ranged from 5 A to 20 A had a calcium-phosphorus product which was never below 40, in some being as high as from 55 to 65. The infants who were given a dilution having a vitamin A potency which ranged from 30 A to 60 A showed no great change in the biweekly determination of the calcium-phosphorus product. This study stressed the rôle of vitamin A in combination with vitamin D in the prophylaxis of rickets in premature and weakling infants, and from that standpoint it is difficult to evaluate the vitamin D factor alone or to compare the results with those of the present study. May and Wygant stated that only 1 infant in their series showed roentgenographic signs of rickets, but they did not mention their criteria for judging the presence of rickets by roentgenogram. Clinical rickets was not observed in their infants.

Drake, Tisdall and Brown,[9] in a study of the relative antirachitic value of cod liver oil, viosterol and irradiated milk, observed 529 infants.

6. Hess, A. F.: The Fate of Various Antirachitics Within the Body, Acta pædiat. **16**:467 (July) 1933.

7. Mazzeo, A.: Ulteriori ricerche sull'azione dell'ergosterina irradiata nella cura del rachitismo, Pediatria **40**:1141 (Nov.) 1932.

8. May, E. W., and Wygant, T. M.: The Prophylactic Use and Tolerance of Haliver Oil with Viosterol in Premature and Weakling Infants, J. Pediat. **4**:227 (Feb.) 1934.

9. Drake, T. G. H.; Tisdall, F. F., and Brown, A.: A Study of the Relative Antirachitic Value of Cod Liver Oil, Viosterol and Irradiated Milk, Canad. M. A. J. **31**:368 (Oct.) 1934.

Of 137 infants who received 1, 2 or 3 teaspoons of cod liver oil daily, moderate or marked rickets developed in 3. Of 186 infants who received 100, 200, 400 and 800 Steenbock (270, 540, 1,080 and 2,160 U.S.P.) units no infants showed clinical or roentgenologic evidence of rickets, either moderate or marked. The observations on these two groups were compared with those on 141 infants who received from 20 to 40 ounces (59 to 118 cc.) of irradiated vitamin D milk containing 35 Steenbock (94 U.S.P.) units in each 20 ounces. No infant in this group showed evidence of moderate or marked rickets. Of the 529 infants, 60 were premature. Of these, moderate or marked rickets developed in 3 as compared with 8 of the 469 full term infants. Drake and his co-workers concluded that 100 Steenbock (270 U.S.P.) units of viosterol are just as efficacious as 800 Steenbock (2,160 U.S.P.) units. They agreed with Hess and Lewis [5] that this number of units of viosterol equals in antirachitic potency 35 Steenbock (94 U.S.P.) units of vitamin D in the form of vitamin D milk. In their summary, Drake, Tisdall and Brown stated that 12.8 per cent of 349 infants examined at the outset of their study showed very slight rickets and 4.5 per cent showed mild rickets. We believe that the appraisal of any antirachitic agent used as a prophylactic should rest on its efficacy in preventing even a mild degree of rickets and that its administration must be begun before any rickets is present.

De Sanctis and Craig,[10] in a study of various antirachitic agents over a five year period, observed 948 infants. The age at which the infants were given the antirachitic substance was not stated. No premature infants were observed. Table 3 is a summary of the agents used, the daily dosage, the number of infants in each group, the percentage of protection and the unitage. All conclusions were based on clinical data, as there were no roentgenographic observations or determinations of calcium and inorganic phosphorus content of the serum. De Sanctis and Craig pointed out that various authors [11] have observed

10. De Sanctis, A. G., and Craig, J. D.: A Five-Year Clinical Study of the Prophylactic Value of Antirachitic Agents: An Analysis of Nine Hundred and Forty-Eight Cases, New York State J. Med. **34**:712 (Aug. 15) 1934.

11. Wilson, S. J., and Seldowitz, M.: Clinical Observations on Craniotabes and Rickets, Am. J. Dis. Child. **29**:603 (May) 1925. De Buys, L. R.: A Clinical Study of Rickets in the Breast-Fed Infant, ibid. **27**:149 (Feb.) 1924. Moore, C. U., and Dennis, H. G.: Craniotabes: Its Prevalence and Significance, ibid. **30**:683 (Nov.) 1925. Barenberg, L. H., and Bloomberg, M. W.: The Significance of Craniotabes and Bowing of the Legs, ibid. **28**:716 (Dec.) 1924. Wilson, M. G.: The Prevention of Rickets: The Influence of the Routine Administration of Cod Liver Oil in the Prevention of Rickets in Infants, ibid. **31**:603 (May) 1926.

that from 23 to 30 per cent of infants who receive no antirachitic agent remain free from rickets. They concluded that cod liver oil (either in liquid or in concentrated form) gives almost complete protection from rickets, that viosterol in any of the dosages used gives only slight protection and that carotene (vitamin A) alone gives no protection but that when the latter is added to vitamin D it increases the protection provided by viosterol. These authors were of the opinion that vitamin A is an important factor in the protection of infants against rickets and that viosterol is ineffective because of its lack of vitamin A. Since roentgenograms were not made, it seems probable that rickets may have been present roentgenographically though not clinically, so that the estimation of the presence or absence of rickets seems open to criticism.

TABLE 3.—*Percentage of Protection with Various Antirachitic Agents (According to De Sanctis and Craig* [10])

Agent	Daily Dosage	Unitage			Number of Cases	Percentage of Protection
		A	D			
		U.S.P.	A.D.M.A.	U.S.P.		
Cod liver oil	3 teaspoons	8,032-13,290	6,642	2,043	100	97
Viosterol 100×	10 drops	.....	7,300	2,246	123	77
Viosterol 250×	10 drops	.....	18,000	5,600	128	81.5
Viosterol 500×	10 drops	.....	36,000	11,200	156	76.8
Cod liver oil concentrate (tablets)	3 tablets	6,300	1,500	492	142	92
Cod liver oil concentrate (liquid)	10 drops	7,668	1,500	492	99	78.5
Carotene (liquid concentrate)	20 drops	3,500	.....	.....	99	79.5
Viosterol and carotene	10 drops each	1,750	36,000	11,200	101	87.5

MATERIAL AND METHOD

All infants in this study except 1 were born at the Sloane Hospital for Women, where they remained under our observation for a varying period, until they reached a weight of approximately 2,250 Gm. One infant (case 27) was born at home and was admitted to the Babies Hospital at the age of 9 days. On discharge, the infants were referred to a follow-up clinic, where they were seen every two weeks or oftener during the experiment. All clinical observations were made by one of us. It was believed that the infants observed in a previous study [1] under identical conditions, who received no antirachitic therapy, might serve for comparison, so that further controls were considered unnecessary. Frequent visits were made to the infants' homes by a social worker to insure that instructions given at the clinic were followed out.

All infants except 2 received breast milk exclusively from the first day of life for varying periods up to several weeks. When necessary, the feeding was complemented by a formula of nonirradiated evaporated milk with added carbohydrate. When weaned, the majority of the infants receive nonirradiated evaporated milk; a few received whole milk. Two infants received nonirradiated evaporated milk from birth, and 1 infant was entirely breast fed throughout the experiment. Solid food was given as follows: cereal at the fourth to the fifth month and vegetables

at the fifth to the sixth month. Eleven infants received egg yolk at the fifth month, none before that age. We believe that the small amount of vitamin D in the egg yolk probably had no appreciable antirachitic effect in this experiment. As in our two previous studies,[12] the mothers were instructed to keep the infants outdoors but were not told to give them sun-baths without clothes.

The viosterol used in this study was a concentrate supplied by the Food and Drug Administration of the United States Department of Agriculture. It was prepared by a commercial manufacturer of viosterol and contained approximately 24,000 U. S. P. units of vitamin D per gram. The Department supplied us with medicine droppers which delivered an average of 22 mg. of the oil solution per drop. Six drops, therefore, would weigh 132 mg. and contain approximately 3,150 (3,168) U. S. P. units of vitamin D. The dose of 6 drops per day was given to the infants at about the eighth day of life. The exact dates on which the administration of viosterol was started is indicated in table 4. The viosterol was administered by dropping it directly onto the tongue of the infant, after which the dropper was replaced in the bottle without washing it. The dosage was continued without variation and without interruption during the period of the experiment, except in 3 infants for whom the dose was doubled at 3½ months. These infants will be commented on later. The viosterol was well taken. No digestive disturbances were noted, even in the early weeks of life.

Roentgenograms of the forearms and wrists were made bimonthly from birth to the age of 4 months and then monthly through the sixth month. The roentgenographic technic was as follows: distance, 38 inches (96.5 cm.); time of exposure, one-sixth second; milliamperes, 60, and kilovolts, 52.

The calcium and the inorganic phosphorus content of the serum were determined monthly throughout the experiment by the methods used in previous studies.[12]

OBSERVATIONS

Clinical Considerations.—The same criteria for the clinical appraisal of rickets have been applied to this group of infants which were used in the two groups studied heretofore. Table 4 shows the prevalence and severity of clinical rickets in the 27 infants studied. Negative findings are represented by blank spaces rather than by zeros. Positive findings are represented in the order of severity on the scale of +, ++, +++ and ++++. Ten infants were free from all clinical evidence of rickets. In the remaining 17 it will be seen that the clinical manifestations varied greatly in different infants but were throughout of the very mildest degree. It is our belief that this amount of rachitic involvement is not significant. It is of interest that in the infant (case 1) who showed the greatest amount of clinical involvement the dose of viosterol was increased to 12 drops (6,300 U.S.P. units) at 3½ months and was further raised to 16 drops (8,190 U.S.P. units)

12. (*a*) Davidson, L. T.; Merritt, K. K., and Chipman, S. S.: Prophylaxis of Rickets in Premature Infants with Vitamin D Milk, Am. J. Dis. Child. **51**:1 (Jan.) 1936.

TABLE 4.—*Observations on Twenty-Seven Premature Infants Receiving Viosterol (3,150 U. S. P. Units)*

Weight and Length at Birth	Date of Birth	Age, Mo.	Clinical Data					Blood Chemistry			Roentgenograms: Degree and Stage of Rickets*	Age Viosterol Begun, Day	Comment
			Rosary	Harrison's Groove	Enlarged Epiphyses	Changes in Cranial Bossae	Craniotabes	Calcium, Mg. per 100 Cc. of Serum	Inorganic Phosphorus, Mg. per 100 Cc. of Serum	Calcium-Phosphorus Product			
Case 1	11/19/34												
R. B.		1	..	..	..	..	..	12.2	7.0	84	E	8	
White		2	..	..	..	..	..	11.3	6.8	71	D		
1,780 Gm.		3	..	..	+	..	+	11.6	6.9	80	B_1		3½ months, viosterol 12 drops per day
44 cm.		4	+	..	++	..	++	11.6	7.1	83	B_1		
		5	+	+	+	+	+	11.2	6.3	71	B_1		5½ months, viosterol 16 drops per day
		6	..	..	+	++	..	12.0	6.2	74	C_1		
Case 2	2/20/34												
B. C.		1	..	..	..	..	..	11.1	7.1	79	E	9	No illness
White		2	..	..	..	..	..	11.3	7.8	88	E		
1,800 Gm.		3	..	..	..	..	..	12.0	7.3	88	B_1		
42 cm.		4	..	..	..	..	..	11.7	6.6	77	C_1		
		5	..	..	..	..	..	11.5	6.8	76	C_1		
		6	..	..	..	..	..	11.5	6.8	78	C_1		
Case 3	8/23/34												
E. C.		1	..	..	..	..	..	11.1	6.5	72	E	8	No illness; not followed after 3 months
White		2	..	..	..	..	..	10.4	6.7	90	E		
1,990 Gm.		3	..	..	..	..	..	....	...	..	B_1		
44 cm.													
Case 4	5/19/34												
F. C.		1	..	..	..	..	..	....	...	..	E	10	No illness
Negro		2	..	..	..	..	..	12.2	5.9	72	E		
2,330 Gm.		3	..	..	..	..	..	11.7	6.2	73	D		
45 cm.		4	..	..	..	..	..	12.0	6.3	74	E		
		5	..	..	..	..	..	11.5	6.6	76	E		
Case 5	6/11/34												
F. D.		1	..	..	..	..	++	10.9	7.4	81	$A_1 O_2$	8	No illness; growth very rapid; not followed after 4 months
Negro		2	+	..	..	..	++	10.9	7.1	77	$C_1 O_2$		
1,560 Gm.		3	..	+	..	..	..	11.9	7.3	87	$C_1 O_1$		
41.5 cm.		4	.	..	..	..	..	11.5	6.2	71	E		
Case 6	7/10/34												
A. E.		1	..	..	..	..	++	10.2	5.6	57	$E O_1$	8	No illness
Negro		2	..	..	..	..	+	11.1	6.5	72	$E O_1$		
2,130 Gm.		3	..	..	..	..	..	12.2	5.9	72	$E O_1$		
45 cm.		4	..	..	..	..	..	12.2	6.0	73	$E O_1$		
		5	..	..	+	..	..	11.5	5.4	62	E		
		6	+	..	+	..	..	....	...	..	E		

Case 7	4/19/34												
C. F.		1	..	..	..	..	..	11.3	6.1	69	E	8	No illness
White		2	..	..	..	..	..	11.3	5.3	60	E		
2,160 Gm.		3	..	..	..	..	..	11.5	6.0	69	B_1		
45 cm.		4	..	..	..	..	..	11.5	6.1	70	B_1		
		5	..	..	..	..	..	11.5	6.1	70	E		
		6	..	..	..	..	..	11.5	5.7	66	..		
Case 8	3/ 1/34												
O. H.		1	..	..	..	..	+++	10.0	5.6	56	E O_1	8	No illness
White		2	..	..	..	..	++	12.0	5.3	64	E O_2		
1,980 Gm.		3	..	..	..	..	..	11.9	6.4	76	D O_2		
44.5 cm.		4	..	..	..	..	..	12.2	5.8	71	E O_1		
		5	..	..	..	..	..	12.1	6.5	79	E		
		6	..	..	..	..	..	....	...	..	E		
Case 9	4/15/34												
D. H.		1	..	..	..	..	..	11.1	6.0	67	E	8	No illness
Negro		2	..	..	..	..	..	11.9	6.4	76	E		
1,610 Gm.		3	..	..	..	..	..	11.3	7.6	86	B_1		
42.5 cm.		4	+	.	..	+	..	11.1	6.5	72	B_1		
		5	+	+	..	+	..	10.9	6.3	69	C_1		
		6	..	+	..	..	..	10.8	6.9	75	C_1		
Case 10	7/6/34												
R. H.		1	..	..	..	..	..	12.2	6.8	83	E	8	
Negro		2	..	..	..	..	..	12.2	7.1	88	E		
2,010 Gm.		3	..	..	..	..	..	12.4	6.2	77	E		
45 cm.		4	..	..	..	..	..	11.5	6.8	78	E		Not followed after 4 months
Case 11	5/ 2/34												
F. H.		1	..	..	..	..	..	10.5	6.8	71	E	8	No illness; growth very rapid
White		2	..	..	..	..	..	11.1	6.7	74	E		
1,640 Gm.		3	..	..	..	..	..	11.9	6.8	81	E		
36.5 cm.		4	..	..	..	..	..	11.9	7.2	86	E		
		5	..	..	..	..	..	11.5	7.3	84	E		
Case 12	6/21/34												
N. H.		1	..	..	..	..	+	11.7	5.6	66	E	10	No illness
White		2	+	+	..	..	+	11.7	6.1	71	D		
2,230 Gm.		3	+	+	..	..	+	11.3	7.0	79	E		
46.5 cm.		4	+	..	+	..	..	12.4	6.9	86	E		
		5	..	..	..	..	..	11.7	6.6	77	E		
Case 13	2/17/34												
R. J.		1	..	..	..	..	++	11.1	6.8	75	E	10	
White		2	..	..	..	..	++	11.5	6.5	73	E		
2,020 Gm.		3	..	..	..	..	++	11.3	6.3	71	E		
44.0 cm.		4	..	..	..	..	+++	11.3	5.5	62	D		German measles at 4 months
		5	..	..	..	..	+++	11.5	6.8	78	B_1		
		6	..	..	..	..	+	11.5	6.2	71	B_1		

* The letters A, B, C, D, E are used to indicate the type of rickets: A, active progressive rickets without evidence of healing; B, the rachitic process in balance, that is, with evidence of healing in the presence of continued activity; C, healed rickets without evidence of activity; D, doubtful rickets, and E, no rickets. The degree of rachitic involvement is graded by the numbers 1, slight; 2, moderate; 3, marked, and 4, severe.

TABLE 4.—*Observations on Twenty-Seven Premature Infants Receiving Viosterol (3,150 U. S. P. Units)—Continued*

Weight and Length at Birth	Date of Birth	Age, Mo.	Clinical Data					Blood Chemistry			Roentgenograms: Degree and Stage of Rickets*	Age Viosterol Begun, Day	Comment
			Rosary	Harrison's Groove	Enlarged Epiphyses	Changes in Cranial Bossae	Craniotabes	Calcium, Mg. per 100 Cc. of Serum	Inorganic Phosphorus, Mg. per 100 Cc. of Serum	Calcium-Phosphorus Product			
Case 14	2/16/34												
B. K.		1	..	..	..	..	..	11.1	6.7	74	E	12	Mild rhinopharyngitis at 2 months
White		2	..	..	..	..	..	....	....	..	E		
1,600 Gm.		3	..	..	..	..	..	11.5	7.5	86	E		
42.5 cm.		4	..	..	..	..	..	11.3	4.2	47	D		
		5	+	..	..	+	..	11.7	6.5	76	A_1		
		6	+	..	..	+	..	12.4	6.0	74	B_1		
Case 15	5/29/34												
M. L.		1	..	..	..	..	..	11.1	7.3	81	E	9	No illness
White		2	..	..	..	..	++	11.3	5.8	65	D		
2,130 Gm.		3	..	..	..	..	+	10.6	6.5	68	B_1		
45 cm.		4	..	..	..	+	+	12.4	6.9	86	B_1		
		5	..	..	..	..	..	11.3	6.7	74	C_1		
		6	..	..	..	..	..	11.7	6.8	80	E		
Case 16	11/10/34												
J. Mc.		1	..	..	..	..	..	....	6.8	..	E O_1	8	Mild hydrocephalus to 3 months, apparently arrested; 3½ months, viosterol 12 drops per day
White		2	..	..	..	..	+	11.3	6.7	76	B_1 O_1		
2,070 Gm.		3	..	..	..	..	++	12.0	6.9	83	B_1		
42 cm.		4	..	..	..	..	++	11.8	7.6	90	B_1		
		5	..	+	..	+	++	11.6	7.3	85	C_1		
		6	..	+	..	+	+	11.4	7.1	81	C_1		
Case 17	11/ 6/34												
H. Mc.		1	..	..	..	..	..	10.9	7.3	80	D	8	No illness; 4 months, viosterol 12 drops per day
White		2	..	..	..	..	..	11.1	7.0	77	A_1		
2,200 Gm.		3	..	..	..	..	..	11.3	6.9	78	B_1		
46 cm.		4	..	+	..	+	..	11.2	5.9	65	B_1		
		5	..	..	..	..	..	11.6	6.9	80	B_1		
		6	..	+	..	..	..	11.4	6.8	78	C_1		
Case 18	1/17/34												
M. A.		1	..	..	..	..	..	11.7	6.7	78	E	9	No illness; not followed after 3 months
Negro		2	..	..	..	..	..	11.5	6.7	76	D		
2,220 Gm.		3	..	..	..	..	..	11.3	7.0	79	E		
45 cm.													
Case 19	1/17/34												
M. B.		1	..	..	..	..	..	11.5	6.3	72	E	9	No illness; not followed after 3 months
Negro		2	..	..	..	..	..	11.5	6.9	79	A_1		
1,820 Gm.		3	..	..	+	++	..	11.1	7.1	79	E		
43 cm.													

Case 20	6/ 2/34												
D. M.		1	..	.	..	..	..	11.1	6.4	71	E	8	No illness
White		2	..	..	..	..	..	11.3	6.4	72	A_1		
1,840 Gm.		3	+	..	..	..	..	10.8	6.7	72	B_1		
44.8 cm.		4	+	..	..	..	..	11.9	6.6	79	B_1		
		5	..	..	+	..	..	12.4	7.1	98	C_1		
Case 21	11/28/34												
D. O'B.		1	..	..	..	..	..	11.3	6.9	78	E	8	Mild furunculosis of scalp at 4 months
White		2	..	..	..	..	+	11.5	6.8	78	D		
2,140 Gm.		3	..	..	..	..	+++	11.8	6.8	80	B_1		
45.5 cm.		4	+	+	..	..	+++	11.4	7.4	83	B_1		
		5	+	+	..	..	..	10.2	7.0	71	B_1		
		6	+	..	..	..	..	....	...	..	C_1		
Case 22	1/ 8/34												
A. P.		1	..	..	..	..	..	11.3	7.3	82	E	21	No illness
White		2	..	..	..	..	..	11.5	6.8	82	E		
2,230 Gm.		3	+	..	..	..	..	11.3	6.6	74	D		
45.5 cm.		4	..	..	..	..	..	11.3	7.5	84	D		
		5	..	+	..	..	..	12.4	7.8	97	E		
		6	..	..	..	+	..	11.7	6.8	80	E		
Case 23	5/ 2/34												
W. P.		1	..	..	..	..	..	11.7	5.5	64	E O_1	8	No illness
White		2	..	..	..	..	..	....	...	..	E O_1		
2,300 Gm.		3	..	..	..	..	..	11.7	6.5	76	A_1 O_1		
45 cm.		4	..	..	..	..	..	11.5	7.3	82	B_1		
		5	..	..	..	..	..	11.1	6.4	71	B_1		
Case 24	9/23/34												
M. R.		1	..	..	..	..	..	11.3	6.6	75	E	8	Moderate anemia at 2 months, given iron; chickenpox at 3½ months; otitis on left side with myringotomy at 5½ months
White		2	..	..	..	..	..	11.5	7.6	86	E		
1,400 Gm.		3	..	..	..	..	..	11.7	8.0	94	E		
38.5 cm.		4	..	..	..	..	..	11.5	7.1	82	E		
		5	..	..	..	..	..	11.8	7.8	92	E		
		6	+	+	..	..	..	....	...	..	...		
Case 25	4/ 3/34												
L. S.		1	..	..	..	..	+	10.7	7.0	75	E O_1	8	Otitis media on left side at 4 months
White		2	..	..	..	..	..	11.7	4.4	51	E O_1		
2,400 Gm.		3	..	+	+	..	..	11.1	6.4	71	A_1 O_1		
45 cm.		4	..	+	+	..	..	12.6	5.6	72	A_1 O_1		
		5	..	..	..	..	..	11.9	5.3	63	B_1		
		6	..	..	..	..	..	11.7	6.3	74	C_1		
Case 26	8/31/34												
R. S.		1	..	..	..	..	..	11.5	6.9	77	E	8	Acute pharyngitis at 3 months
Negro		2	..	..	..	..	..	11.9	6.4	76	E		
2,230 Gm.		3	..	..	..	..	..	11.7	5.3	62	E		
44 cm.		4	..	..	..	..	..	....	5.9	..	E		
		5	..	..	..	..	..	11.9	6.4	76	E		
		6	..	..	..	..	..	....	...	..	E		
Case 27	7/ 7/34												
E. W.		1	..	..	..	..	..	9.6	...	..	E	21	Bronchopneumonia and otitis media at 3 months; in hospital 7 weeks
White		2	..	..	..	..	..	9.8	5.9	58	B_1		
1,590 Gm.		3	..	..	..	..	..	....	...	..	E		
40.5 cm.		4	..	..	..	..	..	11.9	6.7	80	B_1		
		5	..	..	..	..	..	....	...	..	B_1		

without appreciable effect on the physical signs of rickets. It will be noted that the calcium phosphorus products were uniformly high and that roentgenologically there was evidence of rickets of the B type at the third month, which had healed by the sixth month. As will be brought out later, this was a roentgenologic course which was observed in several infants who were free from clinical signs of rickets.

Craniotabes was, in general, more frequently observed in this group than in those previously reported on,[12] but with 1 exception (case 13) it was not more severe. The infant in case 13 showed moderate craniotabes of the physiologic type, that is, occurring at the margins of the cranial bones, from birth through the third month. Thereafter there was increased softening at the centers of the cranial bones without other clinical evidence of rickets but with a simultaneous development of slight roentgenologic evidence of rickets of the B type in the long bones. It is probable that both physiologic and rachitic craniotabes can occur in the same infant and that this infant is an example of such a manifestation.

Chemical Considerations.—Values for the calcium and the inorganic phosphorus content of the serum and their products are shown in table 4. It will be seen that the values were consistently at high normal levels, except in 2 infants. One infant (case 14) showed a slightly low value for inorganic phosphorus (4.2 mg.) at the fourth month, with a slightly lowered calcium-phosphorus product (47). This infant showed minimal clinical involvement, with a 1 plus rosary and bossing at the fifth and sixth months. The other infant (case 25) had a value for inorganic phosphorus of 4.4 mg. at the second month, with a calcium-phosphorus product of 51. These high values for calcium and inorganic phosphorus duplicated closely those observed in our study of infants given 5,000 U.S.P. units per day in the form of viosterol 250 D. They further substantiate our previous conclusions and those of Hess[13] that mild degrees of rickets observed clinically and roentgenologically are not reflected in the values for calcium and inorganic phosphorus in the serum.

Roentgenologic Considerations.—Roentgenologic observations are shown in table 4, where they may be compared with the clinical and chemical observations month by month. As in previous studies, Dr. Martha M. Eliot has given assistance in the interpretation of the roentgenograms and has suggested the use of the letters A, B, C, D and E to indicate the type of rickets, as follows: A, active progressive rickets

13. Hess, A. F.: Rickets, Osteomalacia and Tetany, Philadelphia, Lea & Febiger, 1929.

without evidence of healing; B, the rachitic process in balance, that is, with evidence of healing in the presence of continued activity; C, healed rickets without evidence of activity; D, doubtful rickets, and E, no rickets. The degree of the rachitic involvement is graded by the numbers 1, slight; 2, moderate; 3, marked, and 4, severe.

From a roentgenologic standpoint, 9 of the 27 infants were free from rickets throughout the period of observation. Four of the 9 infants had one doubtful (D) reading but were normal thereafter and were not considered to have had rickets. Serial roentgenograms of 1 such infant (case 26) are shown in figure 1. The bones throughout are normal in contour and of excellent calcium density, and the epiphyseal lines are regular, even and clearly defined. One infant (case 5) showed doubtful (D) rickets at 2 weeks of age and at 1 month had mild active rickets with definite osteoporosis. By the second month, however, the rickets had healed completely, though the osteoporosis

TABLE 5.—*Degree and Stage of Roentgenologic Rickets in Premature Infants Receiving Viosterol (3,150 U. S. P. Units)*

Degree and Stage of Rickets	Age					
	1 Month	2 Months	3 Months	4 Months	5 Months	6 Months
E	25	16	11	9	9	5
D	1	5	3	3	..	..
A_1	1	3	2	1	1	..
B_1	..	2	10	10	7	2
C_1	..	1	1	1	5	7

persisted. By the fourth month the bones were normal. It is to be noted that the infant showed negligible evidence of rickets clinically and that the values for serum calcium and inorganic phosphorus remained at normal levels. The infant was small, and growth in weight and height was very rapid, but these factors seem inadequate as an explanation for the early development of roentgenologic signs of rickets.

In the remaining infants in whom roentgenologic evidence of rickets developed it was consistently mild, usually of the B type, appeared in the majority at the third month and tended to heal satisfactorily by the fifth or sixth month. The typical roentgenologic course could therefore be represented by the following serial month to month readings: E, E, B_1, B_1, B_1, C_1, from birth to 6 months of age. Figure 2 shows such a month to month series of roentgenograms for 1 infant (case 1). It will be noted that the film made at the second month shows a slight irregularity and spurring of the lower end of the ulna. This was read as doubtful rickets, but by the third month the condition had progressed

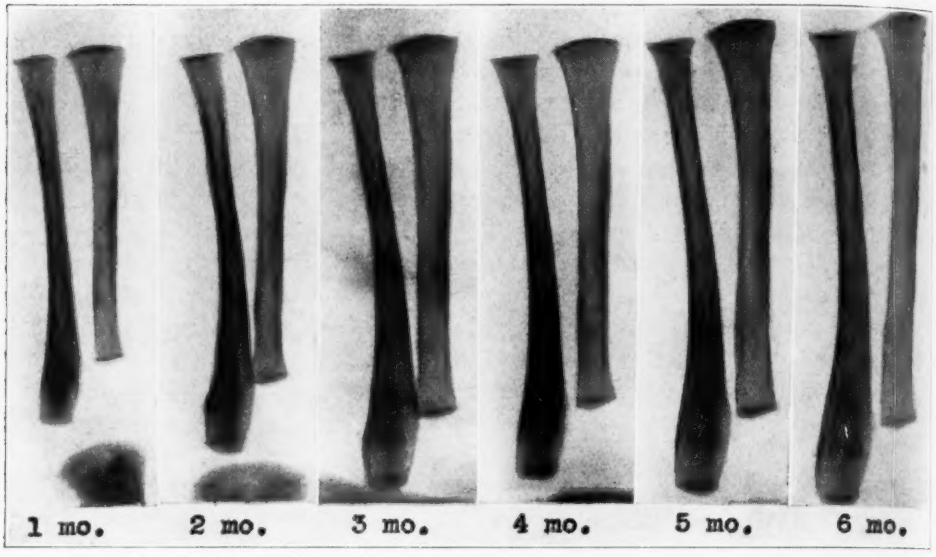

Fig. 1 (case 26).—Absence of roentgenologic evidence of rickets in a premature infant receiving viosterol therapy from birth to 6 months of age.

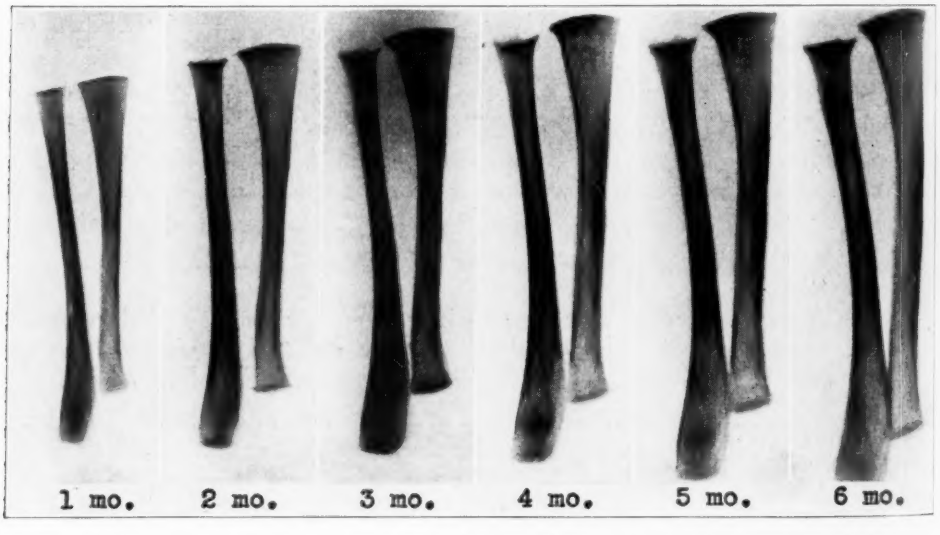

Fig. 2 (case 1).—Development of mild rickets, which healed by the sixth month, in a premature infant.

to slight but definite rickets. Deposition of calcium occurred simultaneously, however, and the bones were designated as showing the B_1 type of rickets until the sixth month, when the lesion seemed to be completely healed (C_1) so far as could be determined by roentgenogram.

As stated previously, this infant (case 1) showed the greatest amount of clinical rickets of any in the group, and the dose of viosterol was doubled (6,300 U.S.P. units daily) at 3½ months of age. The dose was also doubled for 2 other infants (cases 16 and 17). The increased dose may have had some influence on the healing in the 3 infants, as evidenced by roentgenogram at the sixth month. The same degree and rapidity of healing, however, was observed in another infant, whose dose of viosterol remained at the same level throughout the period of observation.

The degree and stage of rickets by months is summarized in table 5. The summary further emphasizes the fact that the greatest amount of roentgenologic evidence of rickets of the B type occurred from the third to the fifth month and that by the sixth month the majority of infants showed bones which were normal or had been the seat of early mild rickets which had healed.

COMMENT

In a recent study [12a] on vitamin D milk as the only source of antirachitic substance we pointed out that a majority of the infants were free from rickets for the first two months and that thereafter mild rickets of the B type developed, which healed by the sixth month. We raised the question whether such a course might not be due to a period early in the infant's life when the intake of vitamin D is inadequate in relation to the impetus for growth. This possibility exists not only for vitamin D milk but for other forms of antirachitic therapy, especially cod liver oil, concerning which the general opinion is that adequate dosage cannot be instituted in the very early postnatal period. In this study the infants received the maximum dose of vitamin D from the eighth day of life, yet they were not completely protected. Is it possible to prevent even the minor degrees of rickets evidenced in this study by beginning vitamin D therapy earlier than was done in these infants or by increasing the dose in the very early days of life? It is our opinion that herein lies the crux of the modern phase of the prophylaxis of rickets. Great advances have been made in therapy in recent years, especially in the standardization of cod liver oil and viosterol and in the perfection of the various forms of milk fortified with vitamin D. Still, mild rickets in the human infant has not been entirely eradicated, and to this end future studies should be directed.

SUMMARY

A group of 27 premature infants were given viosterol, 3,150 U.S.P. units daily, as their sole antirachitic substance in an effort to protect them from rickets.

Ten infants remained free from rickets clinically, and 9 had roentgenologic evidence of rickets.

In the other infants (approximately two thirds of the group), in whom rickets developed, it was consistently mild and healed satisfactorily by the sixth month.

The question is raised whether a greater degree of protection can be attained by more intensive therapy in the early postnatal period.

Case Reports

DEATH FROM HEMORRHAGIC ENCEPHALITIS FOLLOWING TREATMENT WITH SULPHARSPHENAMINE

REPORT OF TWO CASES IN SYPHILITIC INFANTS

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Death from hemorrhagic encephalitis caused by the arsphenamines has been noted from the earliest years of the use of these drugs.[1] Globus and Ginsburg [2] in 1933 were able to list sixty cases, clinically and pathologically well authenticated, the great majority of which were reported from European clinics. To this number they added fourteen other clinically typical cases which lacked pathologic confirmation. There are reports of three nonfatal cases since then.[3] The two cases reported here are the first to be described in infants.

REPORT OF CASES

CASE 1.—S. F., a 5 month old girl, was brought to the Stanford University Hospital on Sept. 10, 1929, because she had been having convulsions of increasing frequency and severity for twelve hours before admission. Three and one-half months previously snuffles, syphilids and a strongly positive Wassermann reaction of the blood had been discovered. At that time the spinal fluid, which was blood-tinged, gave a strongly positive Wassermann reaction and a colloidal gold curve of 3112321000. The Wassermann reaction of the mother's blood was strongly positive.

From the Department of Pediatrics, Stanford University Medical School.

1. Almkvist, J.: Ein Fall von Encephalitis haemorrhagica acuta nach intravenöser Salvarsaninjektion, München. med. Wchnschr. **58**:1809, 1911. Fischer, B.: Ueber einen Todesfall durch Encephalitis haemorrhagica im Auschluss an eine Salvarsaninjektion, ibid. **58**:1803, 1911. von Kannengiesser: Zur Kasuistik der Todesfälle nach Salvarsanbehandlung, ibid. **58**:1806, 1911.

2. Globus, J., and Ginsburg, S.: Pericapillary Encephalorrhagia Due to Arsphenamine: So-Called Arsphenamine Encephalitis, Arch. Neurol. & Psychiat. **30**:1226 (Dec.) 1933.

3. Strohm, J.: Hemorrhagic Encephalitis, Northwest Med. **32**:347, 1933. Netherton, E.: Hemorrhagic Encephalitis (Serous Apoplexy) Following the Administration of Neosalvarsan: Report of Two Cases with Recovery, M. Clin. North America **17**:1005, 1934.

The baby improved rapidly under treatment. She received a course of eight semiweekly intramuscular injections of 0.1 Gm. of sulpharsphenamine (0.017 Gm. per kilogram of body weight), followed by a course of eight semiweekly intramuscular injections of bismidol (0.064 Gm.). Before she received the fifth injection of the second course of sulpharsphenamine, two days before the onset of her present illness, she had shown no evidence of intolerance to treatment.

Forty hours after the last injection of sulpharsphenamine she began to sneeze and to have a nasal discharge. Within twelve hours after these symptoms appeared convulsions began, which increased in frequency and severity until she was brought to the hospital twelve hours later. At that time she was comatose and breathing very irregularly. The fontanel was tense and bulging. There were frequent convulsions and muscular twitchings which appeared to be lateralized more to the right than to the left. The rectal temperature was 38.2 C. (100.7 F.) and rose to 40.1 C. (104.2 F.) just before death. Convulsions, coma and irregular respiration continued till the patient died, six hours after admission. A ventricular puncture and bilateral decompression were of no avail.

Necropsy Report (by Dr. Johnson).—The leptomeninges appeared normal. The brain was soft and somewhat edematous. Microscopic sections showed very marked congestion and large areas of beginning softening. There were numerous small hemorrhages into the brain substance affecting the white matter more severely than the gray. There was a slight diffuse round cell infiltration, but no definite syphilitic lesions were noted in the central nervous system. The rest of the examination revealed nothing of importance. The anatomical diagnosis was hemorrhagic encephalitis due to sulpharsphenamine.

Case 2.—L. A., a boy 12 months of age, was brought to the hospital on May 6, 1935, because he had just had a convulsion. Secondary syphilis had developed in the mother during the fifth month of gestation. Intensive antisyphilitic treatment was begun at once and continued until the time of delivery, with the result that the baby was carried to term. At the time of delivery (which was in another city), the Wassermann reaction of the mother's blood had become negative. When the infant was 6 weeks old the Wassermann reaction of his blood was strongly positive, but he had no other evidence of the infection. He was given ten weekly injections of a soluble bismuth preparation. A rest period of six weeks was followed by another similar course of bismuth, and no other treatment was given till he was brought to the Stanford outpatient department on April 6, 1935.

He was then well developed and well nourished. The only evidences of present or past syphilitic infection were thick phalanges, a suspicious diaper rash and a strongly and repeatedly positive Wassermann reaction of the blood. Roentgenograms of the bones showed no evidence of syphilis.

He was given 0.20 Gm. of sulpharsphenamine (0.018 Gm. per kilogram of body weight) intramuscularly twice a week. The diaper rash promptly healed, and he gained satisfactorily and manifested no intolerance to treatment till the seventh injection was given.

A few hours later he began to sneeze and had a little nasal discharge. The following day he was irritable and cried considerably. The next morning he vomited a number of times, and that night he suddenly had a convulsion, whereupon he was promptly brought to the hospital.

After admission, he showed frequently recurring convulsions, and during the intervals he was limp and stuporous. There were no constant focal neurologic signs. The optic disks were not remarkable except for venous congestion. The

heart rate was markedly accelerated, the respirations were very irregular even between attacks and the rectal temperature was 37 C. (98.6 F.). The results of the blood count and urinalysis were normal. The blood calcium content was 9.69 mg. per hundred cubic centimeters. The Wassermann reactions of the blood and spinal fluid were strongly positive. The spinal fluid was under increased pressure, but its removal was not accompanied by any improvement in the infant's condition. There were four lymphocytes per cubic millimeter of spinal fluid, and the protein content was 284 mg. per hundred cubic centimeters. The colloidal gold curve was 5543333210.

Avertin anesthesia stopped the convulsions temporarily, but the next morning there were marked generalized muscular rigidity, irregular muscular jerking, profound coma and very irregular respiration of the Biot type. The optic disks were markedly edematous, the veins were engorged, and there were a few fresh retinal hemorrhages. The skin and mucous membranes continued to appear normal. The rectal temperature rose to 39.4 C. (102.9 F.) just before death, which occurred eighty hours after the last injection of sulpharsphenamine, seventy-two hours after the onset of symptoms and eighteen hours after the convulsions began. The heart continued to beat for about two minutes after respiration had ceased.

Necropsy Report (by Dr. S. Leland and Dr. J. L. Carr of the San Francisco Coroner's Office).—Macroscopic Examination: The lungs were aerated. The pleural surfaces were smooth, and there was no evidence of pneumonia. Neither was there any fibrosis in the pulmonary parenchyma. The other viscera were entirely normal and well preserved. The brain was normal in size and shape but was edematous. The leptomeninges showed no pathologic changes. The hemispheres were symmetrical, as were the ventricles, but there was hemorrhage in both caudate nuclei, in the right corona radiata and at the bases of both temporal lobes. The vessels in the cortex stood out clearly.

Microscopic Examination: Sections of the brain showed considerable edema and distention of the vessels. There was some fine wrinkling of the ependymal linings. The leptomeninges were moderately edematous, but they bore no exudate. Most of what seemed to be fine petechial hemorrhages when seen grossly were dilated and congested vessels, although there were many areas where blood was found throughout the cerebral cortex. In these areas there was a little thickening of the vessel walls, and there were collars of lymphocytes and leukocytes about them. Sections of the other organs showed no cytologic changes, although the splenic corpuscles were a little more prominent than usual.

The exact nature of hemorrhagic encephalitis is not yet clear. There is no known means of anticipating its occurrence. Treatment by the use of epinephrine, spinal drainage, sodium thiosulphate, sedatives and calcium is of somewhat questionable value. Two nonsyphilitic patients receiving an arsphenamine compound[4] have died, indicating that the accident is not uniformly conditioned by the presence of a syphilitic infection. The agent responsible may act directly on the brain, or the cerebral effects may be the result of primary injury elsewhere in the body. No constant visceral lesions which would suggest impairment

4. Henneberg, R.: Ueber Salvarsan-hirntod, Klin. Wchnschr. **1**:207, 1922

of metabolism or excretion have been found. There are several German reports of hemorrhagic encephalitis following the administration of acetarsone,[5] indicating that arsenical preparations other than the arsphenamines may cause this reaction. Ehrlich expressed the belief that a derivative of the drug, which requires a day or two for liberation in the body, is the most probable cause of the disorder. This would explain the characteristic delay of a few days in the appearance of symptoms. The most widely accepted modern conception is that hemorrhagic encephalitis is the result of an idiosyncrasy.

COMMENT

The injection of sulpharsphenamine was undoubtedly responsible for the death of the two infants whose cases are reported. The clinical course and pathologic changes are the counterpart of those in the descriptions of cases in adults. The first patient described had changes in the spinal fluid characteristic of syphilis of the central nervous system when treatment was started but did not manifest any intolerance to treatment until the onset of hemorrhagic encephalitis three and one half months later. At autopsy no evidence of syphilis was seen in the brain or meninges. The second patient had similar changes in the spinal fluid during the course of the hemorrhagic encephalitis and at autopsy showed fairly definite evidences of meningovascular syphilis. One can draw no definite conclusions from the data as to whether syphilitic inflammation of the central nervous system predisposed the infants to the accident. No other predisposing cause was revealed either clinically or pathologically.

Statistical analysis of the results obtained at the Stanford University Hospital by the use of sulpharsphenamine in the treatment of congenital syphilis during the last fifteen years does not indicate that this drug is more dangerous than other arsenical compounds. On the contrary, except for the two deaths reported here, the results have been satisfactory. In a series of over three hundred cases there have been one case of mild exfoliative dermatitis without loss of hair or nails in a boy of 7 years, two mild cases of jaundice in boys of 8 and 15 and nine cases of mild arsphenamine dermatitis. No dyscrasias of the blood due to sulpharsphenamine have been encountered. Stokes [6] stated that the use of sulpharsphenamine in adults is of questionable justification because this drug has been found to be more prone to cause serious reactions than the other arsphenamines, but he also stated that children tolerate sul-

5. Reiter, G.: Ueber Encephalitis nach Spirozid, Deutsche med. Wchnschr. **58**:1482, 1932.

6. Stokes, J.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

pharsphenamine better than do adults. In four of Cole's[7] six cases of hemorrhagic encephalitis the condition was precipitated by sulpharsphenamine, indicating that, in adults at least, it is in this respect more dangerous than the other arsphenamines. In general, sulpharsphenamine has gradually lost favor in many quarters.[8] However, in young children and in infants for whom treatment with an arsenical compound is indicated and intravenous therapy is not feasible, sulpharsphenamine remains the drug of choice. All serious reactions should be promptly reported so that their incidence may be accurately known, for it is generally accepted that as long as any of the arsphenamines now available are used, there will be an occasional unavoidable severe reaction and death.

In view of the fact that hemorrhagic encephalitis appears to be a matter of individual idiosyncrasy and in a considerable number of cases has occurred after the first injection of an arsphenamine compound, as well as after the administration of acetarsone, these drugs should not be promiscuously used in the treatment of mild nonsyphilitic disorders. Despite their great therapeutic value, treatment with the arsphenamines is, after all, a heroic measure and should not be carelessly employed.

SUMMARY

Two cases of hemorrhagic encephalitis in syphilitic infants receiving sulpharsphenamine are reported with autopsy observations.

The clinical syndrome and the pathologic changes were the counterpart of those reported in cases in adults.

Sulpharsphenamine is probably more prone to produce hemorrhagic encephalitis and other severe reactions in adults than are the other arsphenamines, but it is a very satisfactory drug for the treatment of syphilis in infants and children.

The remote but definite possibility of hemorrhagic encephalitis should be borne in mind when an arsphenamine is used in the treatment of mild nonsyphilitic disorders.

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7. Cole, H. N., and others: Toxic Effects Following Use of the Arsphenamines, J. A. M. A. **97**:897 (Sept. 26) 1931.

8. Sulpharsphenamine: Its Uses and Limitations, report of the Council on Pharmacy and Chemistry, J. A. M. A. **99**:1688 (Nov. 12) 1932.

INFLUENZAL MENINGITIS WITH RECOVERY

USE OF ANTI-INFLUENZAL SERUM

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DURHAM, N. C.

The use of anti-influenzal serum with complement offers a hopeful method for the treatment of influenzal meningitis, a disease which has a high mortality. Neal, Jackson and Applebaum [1] listed thirty-five reported cases of recovery up to February 1934, including four cases of their own. Eight of the patients received anti-influenzal serum. The recovery in four of the eight cases could not be ascribed to the use of the serum. Three more cases of recovery,[2] not listed by Neal and her associates, were reported in the literature prior to 1934. Since February 1934, there have been five more recoveries,[3] including the one reported here. Of the eight patients, only two (Rittenberg's [3b] and mine) received anti-influenzal serum. For both, complement [4] was used with the serum. Repeated spinal taps and other nonspecific measures were used in most of the cases of recovery reported.

From the Department of Pediatrics, University of Oregon School of Medicine, and the Doernbecher Memorial Hospital for Children.

1. Neal, J. B.; Jackson, H. W., and Applebaum, E.: Meningitis Due to the Influenza Bacillus of Pfeiffer (Hemophilus Influenzae): A Study of One Hundred and Eleven Cases, with Four Recoveries, J. A. M. A. **102**:513 (Feb. 17) 1934.

2. Martmer, E. E., and Davidson, E. C.: Surgical Treatment of Spinal Block: Report of a Case of Pfeiffer's Bacillus Meningitis Treated by Open Drainage, J. Michigan M. Soc. **30**:936 (Dec.) 1931. Roberton, H. E. W.: Case of Pfeiffer Meningitis with Recovery, St. Barth. Hosp. J. **40**:10 (Oct.) 1932. Paisseau, G.; Tournant, P., and Patey, G.: Méningite à bacille de Pfeiffer chez un nourrisson, Bull. Soc. de pédiat. de Paris **31**:93 (Feb.) 1933.

3. (*a*) Duncan, D. H., and Webb, C. H.: Recovery from Influenzal Meningitis, J. Pediat. **4**:216 (Feb.) 1934. (*b*) Rittenberg, B. B.: Influenzal Meningitis: Report of a Case with Complete Recovery, J. A. M. A. **102**:1674 (May 19) 1934. (*c*) Dyke, S. C., and Little, C. J. H.: Meningitis Due to Bacilli of Pfeiffer Type, Lancet **1**:1392 (June 30) 1934.

4. (*a*) Ward, H. K., and Wright, J.: Studies on Influenzal Meningitis: I. The Problems of Specific Therapy, J. Exper. Med. **55**:223, 1932. (*b*) Ward, H. K., and Fothergill, L. D.: Influenzal Meningitis Treated with Specific Antiserum and Complement: Report of Five Cases, Am. J. Dis. Child. **43**:873 (April) 1932.

REPORT OF A CASE

An American girl of 6 years was admitted to the hospital on March 20, 1935, in a state of unconsciousness. She had been well until March 15. At this time she seemed slightly "hysterical" after hard play at a friend's home. She was kept quiet at home during the following three days. On March 19 she attended school. At noon of March 20 the child complained of a severe frontal headache and was very tired. At 5 p. m. she vomited repeatedly. At 6 p. m. the headache ceased, and the patient became more and more drowsy and lapsed into a state of coma. She was sent into the Doernbecher Memorial Hospital for Children at 11 p. m. by Dr. Merl L. Margason.

Observation on Spinal Fluid and Serum Administered During the Period in the Hospital

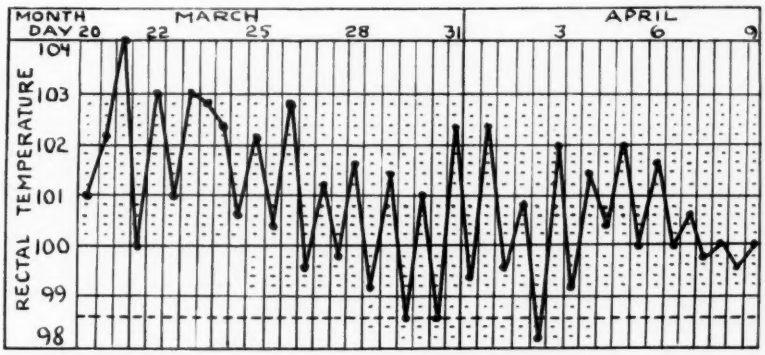
							Serum			
							Amount Given, Cc.			
Dates	Cell Count	Appearance	Globulin	Protein, Mg. per 100 Cc.	Organism in Smear	Culture	Antimeningococcic	Antiinfluenzal	Fresh Human	Route*
March 20	4,700	Cloudy	+	.....	?	No growth	15	..	..	I. S.
21 a.m.	3,050	Cloudy	+	53.5†	None seen	B. influenzae isolated on March 25				
p.m.	.....	.....	..	.....	Gram-negative rods	.....	15	..	..	I. S.
p.m.	.....	.....	..	.....	.....	.....	..	15	5	I. S.
22 a.m.	2,550	Cloudy	+	49.5	Occ. gram-neg. rod	No growth	..	25	6	I. S.
p.m.	12,400	.....	+	68.0	.....	.....	..	10	4	I. S.
23 a.m.	5,750	Cloudy	++	140.0	None found	B influenza	..	15	5	I. S.
p.m.	.....	.....	..	.....	.....	.....	..	10	5	I. S.
24 a.m.	17,000	Cloudy	++	.....	.....	.....	..	10	5	I. S.
25 p.m.	1,600	Cloudy	++	55.0	Occ. gram-neg. rod	.....	..	15	5	I. S.
26 p.m.	1,500	Slightly cloudy	+	33.0	.....	.....	..	15	5	I. S.
28	106	Clear	0	29.5	.....	.....	..	15	5	I. S.
29	8	Clear	0	Less than 10	.....	.....	..	15	5	I. S.
31	700	Slightly cloudy	..	.....	.....	.....	..	10	10	I. S.
April 1	14	Clear	0	65.0‡	None found	No growth	..	30 15	8 ..	I. C. I. M.
3	.....	Slightly bloody	..	.....	None found	No growth	..	15	6	I. C.
4	40	Slightly bloody	0	.....	None found	No growth	None given			
8	.....	Bloody	..	.....	None found	No growth	None given			

* I. S. indicates intraspinally; I. C., intracisternally; I. M., intramuscularly.
† The chloride content was 660 mg. per hundred cubic centimeters.
‡ The chloride content was 650 mg. per hundred cubic centimeters; the sugar content, 40 mg.

The patient had mumps in January 1935 and had had an occasional cold. Her tonsils and adenoids had been removed. Physical examination revealed a well developed, well nourished, comatose child. The temperature was 101 F., the pulse rate 70 and the respiratory rate 16. The skin was clear. There was no local or general glandular enlargement. The skeleton was normal. There was spontaneous vertical nystagmus. The eyes were turned occasionally to the right. The pupils

reacted to light. The eyegrounds were normal. The ear drums showed their normal luster. The tongue was coated. The pharynx was moderately inflamed. The heart, lungs and abdomen were normal. The neck was rigid. The Brudzinski and Kernig signs were present. The tendon reflexes were active.

Lumbar puncture was done immediately on admission. The fluid was under definitely increased pressure. Thirty cubic centimeters of cloudy fluid was withdrawn. It contained globulin (+) and 4,700 cells per cubic millimeter, all of which were polymorphonuclear neutrophils. Questionable organisms were seen in the smear stained by Gram's method. Fifteen cubic centimeters of antimeningococcic serum was given intraspinally. On the following morning, March 21, the patient was conscious but hyperirritable and uncooperative. Lumbar puncture was done, cloudy fluid being removed, and 10 cc. of antimeningococcic serum was given. The same procedure was repeated in the afternoon. The smear made from the fluid withdrawn in the morning showed no organisms. A smear made from the fluid withdrawn in the afternoon showed gram-negative rods. A third lumbar tap was done. After the removal of spinal fluid, 15 cc. of anti-influenzal serum [5] and 5 cc. of fresh, human serum giving a negative Wassermann reaction



Temperature curve over a period of twenty-one days in a case of influenzal meningitis.

were injected by gravity. This procedure was repeated twice daily, as indicated in the chart, until clinical and laboratory findings were definitely improved, and then once daily for several days. Cisternal instead of lumbar punctures were done later in the course because a dermatitis due to iodine had developed over the skin of the lumbar area.

B. influenzae was isolated on March 25 from the spinal fluid withdrawn on March 21. It was again cultured from the spinal fluid withdrawn on March 23.

On March 23, the fourth day in the hospital, the child's general condition was unchanged, but she was much more cooperative, and during the next few days there was definite improvement in the rigidity of the neck, mental aspect and spinal fluid cell count. On March 28, the eighth day in the hospital, the spinal fluid cell count was 106, 98 per cent of the cells being polymorphonuclear neutrophils. Because of the possibility of a relapse,[6] the anti-influenzal serum plus

5. Obtained from the Massachusetts Department of Public Health through the courtesy of Dr. LeRoy D. Fothergill.

6. Fothergill, L. D.: Personal communication to the author.

human serum was given once daily or every other day for five more injections. Ten cubic centimeters of serum was given intramuscularly on April 1 because of continued fever. This caused no appreciable change in the child's condition or temperature curve. On the twentieth day in the hospital the temperature had returned to normal, the patient was clinically well, and the spinal fluid cell count was 40. The white blood cell count on March 29 was 7,350, with 46 per cent polymorphonuclear neutrophils. The urine was normal.

The patient was discharged on the twenty-sixth day of hospitalization. She was seen four weeks later. Except for an infrequent frontal headache coming on after hard exercise, she felt well. The physical examination at this time gave entirely negative results.

JUVENILE OSTEOMALACIA

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The diagnosis of juvenile osteomalacia as an entity apart from juvenile rickets has its proponents and opponents. Hess [1] personally felt that the difference in the pathologic lesions is quantitative rather than qualitative and that the underlying pathologic process is the same although there is as yet no satisfactory explanation for the softening of bone which forms so characteristic a phenomenon in osteomalacia.

ETIOLOGY

Locke [2] classified the various forms of osteomalacia with regard to age and etiology as follows:

1. The puerperal form occurs particularly in women who have had numerous and frequent pregnancies. The maternal pelvis, spine and femurs are particularly attacked by the disease. In this form the calcium content of the blood is low and tetany is common. Because of the association of this type with pregnancy, ovarian dysfunction has in the past been thought to be the cause of the disorder and oophorectomy has been resorted to in order to cure the disease. Miles and Feng [3] found that pregnancy and lactation were not absolutely essential factors and that functioning of the ovaries or menstrual activities did not play a major part in the disease.

2. There is probably no reason for separating the nonpuerperal from the puerperal form of this disease. In the former also the blood calcium content is usually low and tetany common. It is probable that with pregnancy this type is made more active, then becoming the puerperal form. It may be cured by adequate doses of fat-soluble vitamins and balanced diet.

3. Hunger osteomalacia, osteopathy or war osteomalacia is characteristically an osteoporosis. Several members of both sexes of the same family may be affected. Tetany is frequently associated with this type.

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1. Hess, A. F.: Rickets Including Osteomalacia and Tetany, ed. 1, Philadelphia, Lea & Febiger, 1929, chap. 13, p. 331.

2. Locke, E. A., in Christian, Henry A., and Mackenzie, James: Oxford Medicine, London, Oxford University Press, 1921.

3. Miles, L. M., and Feng, Chih-Tung: Calcium and Phosphorus Metabolism in Osteomalacia, J. Exper. Med. **41**:137 (Jan.) 1925.

Dalyell and Chick [4] found this type of osteomalacia particularly in middle-aged and elderly persons. They showed that recovery occurred following the addition of fat to the diet, cod liver oil producing the most rapid recovery. Hess [1] pointed out that the important factor in this type of osteomalacia seems to be the duration rather than the intensity of the nutritional deprivation. An adequate diet cures the disease, and because of this I see no reason for separation of this form from forms 1 and 2.

4. The senile form has been recorded in few instances and is characterized by its mild chronic course. It is looked on by some as a bone neoplasm and by others as an osteoporotic process, in which the catabolism of the aged bone is not followed by deposition of new osteoid tissue. Decourt and Kaplan [5] reported three cases in which the condition seemed to be of this type, in all of which the patients responded to treatment with irradiated ergosterol. If senile osteoporosis responds to this therapy, it seems reasonable to class it with the three preceding forms.

5. Juvenile osteomalacia appears, as its name implies, in early adolescence, in both boys and girls. Owing principally to the influence of Hess, it has been confused with juvenile rickets in recent years. I wish to report a case of this type. This form appears to be uncommon in this country. Vedel and Puech [6] reported a case in a 10 year old boy who had apparently been a normal child. This boy showed generalized osseous and muscular atrophy. The calcium content of the serum was high, and tetany was not present. Treatment, including the administration of cod liver oil, had no effect. This appears to be a true case of juvenile osteomalacia. Peron and Meslay [7] reported a case in a 15 year old girl with atrophy of the bones, most marked in the spine and thorax, and general muscular atrophy. Tetany was not present. Treatment had no effect. This may have been a case of juvenile osteomalacia. Dwyer and Eckelberry [8] reported two cases. There are many other reports to be found in the literature, such as that by Locke and those of Hutinel, Gayet and Bonnet, Bernard, and Bossi, as discussed by Molcho,[9] but the cases appear to be instances of rachitic forms of osteo-

4. Dalyell, E. J., and Chick, H.: Hunger-Osteomalacia in Vienna, 1920, Lancet **2**:842 (Oct. 22) 1921.

5. Decourt, J., and Kaplan, S.: The Treatment of Osteomalacia with Irradiated Ergosterol, Paris méd. **2**:485 (Dec. 3) 1932.

6. Vedel, M., and Puech, M.: Un cas d'ostéomalacie masculine apparue à l'age de 10 ans, Arch. franco-belges de chir. **27**:398 (May) 1924.

7. Peron, A., and Meslay: Un cas d'ostéomalacie chez une fillette de 15 ans, Rev. mens. d. mal. de l'enf. **13**:178, 1895.

8. Dwyer, H. L., and Eckelberry, O. S.: Osteomalacia in Children, Am. J. Dis. Child. **31**:639 (May) 1926.

9. Molcho, M.: Osteomalacia Especially in Childhood, Internat. Clin. **2**:187, 1922.

malacia because of the limitation of the process of certain bones, a low blood calcium content, response to specific therapy and so forth.

There are then five reported cases in the available literature, including the one to be described here and one reported by Vedel and Puech, one by Peron and Meslay and two by Dwyer and Eckelberry, that appear to be cases of true juvenile osteomalacia. Hess, compiling data from Stapleton's [10] figures, showed that the relationship in India between osteomalacia and puberty is even closer than that between osteomalacia and pregnancy, but the eastern or oriental form of juvenile osteomalacia responds to specific therapy whereas the type met with in northern latitudes does not. For this and other reasons, I am forced to believe that there are two distinctly separate conditions: the one an osteomalacic process of late rickets, the other a separate entity.

In the case to be presented and the cases cited by Dwyer and Eckelberry, there appears to be no evidence of dietary deficiency, lack of hygienic care or glandular dyscrasia. No therapy has been of any use. The blood calcium content in cases of this type is normal or high. Tetany is not present. Jones and Lovett [11] stated that "true idiopathic osteomalacia in a serious form occurs occasionally in children and is distinct from rickets in the absence of epiphyseal changes characteristic of the disease."

DIAGNOSIS

The diagnosis of juvenile osteomalacia may be said to be established when a condition of rarefaction, softening and atrophy of the bones exists in a child at or near puberty and all other considerations have been ruled out, particularly hyperparathyroidism and juvenile rickets. The latter would seem to be ruled out by therapeutic tests.

In a differential diagnosis the following disease or disorders are to be considered: (1) juvenile rickets; (2) Paget's disease, osteitis deformans; (3) pituitary basophilism, Cushing's disease; (4) osteogenesis imperfecta, fragilitas ossium, osteopsathyrosis; (5) syphilitic osteitis; (6) congenital syphilis; (7) anterior poliomyelitis; (8) renal rickets; (9) celiac rickets; (10) hyperparathyroidism, osteitis fibrosa cystica multiplisata, Recklinghausen's disease; (11) multiple myeloma.

Juvenile Rickets.—The etiology of this disorder is the same as that of infantile rickets, that is, lack of sunlight or a diet deficient in vitamin D, resulting in a disturbance of calcium metabolism. Pain is a common symptom. There is a slight degree of epiphyseal enlargement, and microscopic studies may show overdevelopment of osteoid tissue, which

10. Stapleton, G.: Late Rickets and Osteomalacia in Delhi, Lancet **1**:1119 (May 30) 1925.

11. Jones, R., and Lovett, R. W.: Orthopedic Surgery, New York, William Wood & Company, 1923, p. 389.

when found is accepted as pathognomonic of rickets. Tetany is a frequent accompaniment as the calcium content of the blood is low. Patients with this condition are cured with adequate diet and antirachitic treatment.

Paget's Disease, Osteitis Deformans.—This is a chronic disease of bone occurring in adults, usually between the ages of 50 and 80. It is an osteomyelitis fibrosa and consists of the formation of a solid cellular connective tissue which replaces the bone substance and fills the medullary cavity. The bones of the skull thicken and enlarge but are spongy and may be pliable owing to lack of calcium. The destruction of bone is accomplished not only by the osteoclasts but also by invading blood vessels.

Pituitary Basophilism, Cushing's Disease.—Cushing's disease [12] is characterized by a rapidly acquired plethoric adiposity affecting the face, neck and trunk. The bones may show mottling and enlargement of the trabeculae with thinning of the cortex. The vertebrae may show compression and osteoporosis. It is associated in women with hypertrichosis, amenorrhea and vascular hypertension, with purplish striae distensae of the abdomen and acrocyanosis with cutis marmorata of the extremities. The disease is believed to be due to basophilic tumor of the pituitary, but since the basophilic cells of the pituitary are believed to be responsible for secondary sexual development, the presence of amenorrhea in the syndrome requires further elucidation.

Osteogenesis Imperfecta, Fragilitas Ossium, Osteopsathyrosis.—The disease is both hereditary and congenital. The osteoblasts of the internal and external periosteum form an imperfect type of bone. As the epiphyseal cartilages function normally the bones are of normal length or nearly so, but the medullary cavity is large and the shaft thin, porous and very fragile. Fractures may occur and heal even before birth. It is a disease of early life and if the patient survives, the fragility may last for years or may gradually disappear.

Syphilitic Osteitis.—This disease usually begins in the periosteum, which becomes thickened and infiltrated with cells with or without gumma formation. As the disease progresses, the channels in the bone enlarge by a rarefying osteitis and coalesce, forming large irregular defects filled with new fibrous tissue. Syphilitic osteitis is most frequent in the cranial bones but may be found elsewhere. The Kahn and Wassermann reactions of the blood are positive.

Congenital Syphilis.—The characteristic lesions of this disease are found in the bones at the borderline between the ossifying and the

12. Cushing, H.: Further Notes on Pituitary Basophilism, J. A. M. A. **99**: 281 (July 23) 1932.

calcifying zone. The line between these zones is normally straight, but in syphilis it becomes broader and uneven and presents various modifications which may merge into each other so that all intermediate forms may be seen. The cartilage is soft and almost gelatinous and may contain numerous blood vessels or islets of connective tissue or of irregular calcification.

Anterior Poliomyelitis.—This is essentially a destructive process of the ganglia of the anterior horn cells of the spinal cord and certain areas of the brain stem. The effect in bone is a simple atrophy of disuse following a flaccid paralysis of the skeletal muscles. The diagnosis is established with the finding of the characteristic flaccid paralysis. Similar atrophy of the bones is seen sometimes during prolonged healing of extensive fractures in the extremities.

Renal Rickets, Renal Infantilism or Renal Dwarfism.—This is a form of disturbed calcium metabolism due to the action of one or more retention products which the diseased kidneys are unable to excrete. The ends of the long bones, especially those of the legs, show the exaggerated malformation occurring in florid infantile rickets or infantile osteomalacia. In addition to skeletal involvement and often preceding it there may be marked polyuria and polydipsia. The urine is of low specific gravity and may contain albumin but is usually free from casts. The calcium and the phosphorus content of the blood are high. The kidneys are very small and show advanced interstitial nephritis with marked destruction of the parenchyma. There is no specific therapy.

Celiac Rickets.—This is a disturbance of calcium metabolism showing rachitic epiphyseal changes in osteoporotic bone, which in turn is the result of inability of the intestines to absorb calcium. Tetany is occasionally present. Specific antirachitic therapy seems to have no great effect, if any.

Hyperparathyroidism, Osteitis Fibrosa Cystica Multiplisata or Recklinghausen's Disease.—This is usually due to a functioning adenoma of the parathyroid glands. It may be due to hyperplasia of the parathyroids. Albright, Aub and Bauer[13] described six clinical types, as follows: (1) classic hyperparathyroidism, in which skeletal symptoms predominate, consisting of decalcification cysts, tumors and eventually fractures; (2) the osteoporotic form, in which there is simply skeletal decalcification without cysts or tumors; (3) hyperparathyroidism with renal insufficiency (nephrocalcinosis); (4) hyperplasia with nephrolithiasis in which the presenting symptoms are associated with renal stones and there may be no gross skeletal changes; (5) acute parathyroid poisoning, producing sudden death and characteristic pathologic

13. Albright, F.; Aub, J. C., and Bauer, W.: Hyperparathyroidism, J. A. M. A. **102**:1276 (April 21) 1934.

changes; (6) hyperparathyroidism simulating or complicated by Paget's disease. The diagnosis of this disease rests on the finding of an increased serum calcium level, a decreased serum phosphorus level, increased excretion of both elements in the urine and the demonstration at operation or autopsy of a parathyroid adenoma or hyperplasia. The duration of the disease is prolonged, probably extending over years, and a fatal issue usually occurs from renal involvement.

Multiple Myeloma.—This is a neoplastic disease of bone marrow producing a general or local osteoporosis which may simulate the rarefaction of hyperparathyroidism. The calcium content of the blood may be normal or high and the phosphorus content normal or slightly elevated. Final diagnosis rests on a biopsy of the affected bone with demonstration of the myeloma.

PROGNOSIS

The prognosis of juvenile osteomalacia can be based only on the few cases reported. The patient whose case is to be described died after an illness of exactly twenty-two months. In the two cases reported by Dwyer and Eckelberry, one patient remained unimproved during the time she was under observation; the other was bedfast with severe deformities of the legs. In the cases reported by Vedel and Puech and by Peron and Meslay the condition was not influenced by treatment.

TREATMENT

There appears to be no specific treatment for juvenile osteomalacia. The antirachitic vitamin D alone or in association with vitamin A has no effect, although Hess [1] listed "the therapeutic agents which are specific for osteomalacia, namely, cod liver oil, irradiated ergosterol and ultra-violet irradiation." The osteomalacia referred to is of course rachitis tarda or late or juvenile rickets with osteomalacic changes in the bones. Added calcium administered by mouth or by hypodermic injection does not change the picture. Amino-acetic acid in the case to be presented had a peculiar effect in promoting gain in weight. Passive motion and massage and irradiation with a quartz mercury vapor lamp had no effect on the bony rarefaction. Castration has not been tried in a case of juvenile osteomalacia that I know of, and in view of the conflicting evidence it is probably not justified.

REPORT OF A CASE

History.—Loraine McM. was born on May 16, 1923. The weight at birth was 7 pounds (3,175 Gm.), and delivery was spontaneous, with no evidence of injury, cyanosis or asphyxia. The child was bottle fed from birth on cow's milk and granulated sugar. No antirachitic substance or orange juice was given at any time. Vegetables and cereal were not given until some time between the first and the second year.

The mother was alive. Her thyroid gland had been enlarged for at least nine years. Her father died accidentally and her mother of senility at 67 years of age. The child's father was alive and well. One of the father's brothers died of pulmonary tuberculosis and one of his sisters of tuberculous meningitis; these deaths occurred eighteen years previously. The father's parents died of old age as far as is known.

The child sat alone at approximately 10 months and walked at approximately 17 months. Her first tooth erupted at approximately 13 months. She had measles at 4 years of age and whooping cough and chickenpox in her fifth year.

Present Illness.—The patient was sent home from school in October 1932 because of a streptococcic sore throat. She had no fever at any time, felt well and returned to school in three days. On Nov. 9, 1932, she came home after school and went upstairs to bed of her own volition. Two or three days later she felt well enough to get up and dress but complained of painful feet. She continued to complain of painful feet and later of pain in the back until Jan. 27, 1933, when her tonsils and adenoids were removed. She was dressed and up but getting around only with assistance until May 1933, when she fell; since then she has not attempted to get up. On June 15, 1933, she came to the orthopedic clinic and was made an inpatient. Roentgenograms taken of the spine showed a marked loss of calcium in the vertebrae. On July 6, the calcium content of the blood was 9.97 mg. and the phosphorus content 4 mg. per hundred cubic centimeters. On July 25 she was put on a Bradford frame, where she remained up to the time of her death. On Nov. 1, 1933, she was sent to the Harper Hospital, Detroit, for examination by Dr. Max Ballin and Dr. P. K. Morse, who gave the following report: "The roentgen findings in this case were those of widespread demineralization of bone without cystic areas. At operation no enlarged parathyroid or parathyroid tumors were found. Frozen sections of some of the material removed at operation revealed one small parathyroid island enclosed in a mass of fat. The careful sections made later showed that most of the material removed at operation was of a peculiar type, much more immature than the age of the patient would warrant. It will be noted from the case record that there was no adequate basis for a diagnosis of parathyroidism."

On January 22, the patient contracted otitis media on the right side; the drum ruptured spontaneously. There was no rise in temperature. The ear discharged until February 2. Roentgenograms were taken of the bones on January 25. These showed an increasing atrophy. On Jan. 25, 1934, I was asked to supervise the medical care of the child.

Physical Examination.—While the patient was well nourished in appearance, the distribution of fat was abnormal in that the buccal and cervical fat and that of the extremities was scanty, while there was a noticeably thick abdominal panniculus. The results of the physical examination were essentially negative except for the presence of otitis media and the condition of the extremities. The arms were symmetrical but showed decided absence of fat. The muscles were hypotonic and moderately atrophied. Coordination was good, and movements were normal. The legs were symmetrical but showed more muscular hypotonia and atrophy than the arms. The absence of fat was conspicuous. There was no evidence of paralysis, but the patient was very much disinclined to move the legs. All tendon reflexes were present, equal and diminished. The patient complained of pain in her ankles on movement of the feet.

Roentgen examination made on the same day gave the following results: anteroposterior films of the lower half of the thoracic vertebrae, lumbar vertebrae,

pelvis and upper third of each femur showed marked absence of lime salts in all bones. One lateral film was taken of the right side of the skull. The teeth appeared to be well developed. The tables of the skull showed bony atrophy.

The condition was diagnosed as osteomalacia with muscular hypotonia and atrophy of disuse and suppurative otitis media on the right side.

Laboratory Examination.—Urinalysis showed no pathologic changes. The Kahn reaction of the blood was negative; the Mantoux reaction with 0.1 mg. of old tuberculin was negative. The calcium content of the blood was from 7 to 12 mg. and the phosphorus, 4.7 mg. The basal metabolism was —6 per cent.

Calcium Metabolism: From July 5, 1933, to June 1, 1934, sixteen derterminations of the calcium and phosphorus content of the blood were made. The calcium content as determined was invariably normal or high and the phosphorus content within normal limits. The patient showed no symptoms of tetany, which was in agreement with the calcium content of the blood as found. The determinations of blood calcium were made according to the method of Clark and Collip,[14] and those of blood phosphorus, according to the method of Fisk and Subbarrow.[15]

From Nov. 3, 1933, to July 4, 1934, seven determinations of calcium and phosphorus in the urine were made. McCrudden's [16] method was used to determine the calcium, and that of Fisk and Subbarrow,[15] the phosphorus. Except on March 20, the amount of calcium in the urine was below normal. The phosphorus content of the urine was low in the first three determinations and within normal limits in the remainder. Four determinations of the calcium balance were made from Feb. 2 to July 8, 1934. The first experiment showed a large excretion of calcium in the feces, 8.4 Gm. daily average, and a negative balance of both calcium and phosphorus. The urinary and fecal calcium were determined by McCrudden's [17] method, and the phosphorus, after ashing, by Fisk and Subbarrow's [15] method. The negative balance was still present at the second determination. It was at the time of the first determination of calcium balance that the roentgenogram of the bones showed more rapidly advancing rarefaction. The last two determinations showed a slightly positive balance for both calcium and phosphorus. A healing spontaneous fracture of the left femur might be responsible in some measure for this. The daily fecal excretion of calcium varied from a higher value, of 8.4 Gm., in February to a low value, of 1.2 Gm., in July.

Basal Metabolism: Three determinations of the basal metabolic rate were made. These showed no pronounced deviation. What difference from the normal was found was toward the deficiency side, while the two values for blood cholesterol were at the lower limits of normal. The blood cholesterol was determined after the method of Castellano and Torres.[18]

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14. Clark, E. P., and Collip, J. B.: A Study of the Tisdall Method for the Determination of Blood Serum Calcium with Suggested Modifications, J. Biol. Chem. **66**:375, 1925.

15. Fisk, C. H., and Subbarrow, Y.: The Colorometric Determination of Phosphorus, J. Biol. Chem. **63**:461, 1925.

16. McCrudden, F. H.: The Quantitative Separation of Calcium and Magnesium in the Presence of Phosphates and Small Amounts of Iron Devised Especially for the Analysis of Foods, Urine, and Feces, J. Biol. Chem. **7**:83, 1909-1910.

17. McCrudden, F. H.: The Determination of Calcium in the Presence of Magnesium and Phosphates: The Determination of Calcium in Urine, J. Biol. Chem. **10**:187, 1911-1912; footnote 16.

18. Castellano, J., and Torres, I.: Cholesterol, Clinical Methods of Its Determination and Normal Values, An. Soc. españ. de fís. y quim. **30**:384, 1932.

Other Laboratory Examinations: The urine occasionally showed acetone and diacetic acid. Hyaline and granular casts were found on four occasions. Albumin was found in minimal amounts at five examinations. Two determinations a month apart of the nonprotein nitrogen content of the blood gave 32.0 and 49.9 mg. per hundred cubic centimeters, respectively. The two Kahn tests of the blood for syphilis gave negative results. A determination of the blood sugar after fasting showed 90.9 mg. per hundred cubic centimeters. Repeated blood counts revealed moderate secondary anemia, with an average of 2,500,000 red blood cells; the white

Fig. 1.—Roentgenogram of the knee joints taken in August 1933.

blood cells showed no deviation from the normal. Erythrocyte sedimentations were 27 and 28 mm. in sixty minutes, after Cutler's [19] method. The urea nitrogen content of the urine was determined according to Van Slyke and Cullen's [20] procedure.

19. Cutler, J.: Finger Puncture Method for the Blood Sedimentation Test, Am. J. M. Sc. **173**:687 and 864, 1927.

20. Van Slyke, D. D., and Cullen, C. E.: The Determination of Urea by the Urease Method, J. Biol. Chem. **24**:117, 1916.

Roentgen Examination.—The first films were taken on June 29, 1933, and at intervals from then until Sept. 4, 1934. From January 1934 the atrophy of the bones became more pronounced. Dr. H. H. Pool, the roentgenologist, made the following comment: "A review of all the films taken of this patient demonstrates a gradual but progressive absorption of lime salts in all bones. This was quite well advanced at the original examination. In the later film the bony structure appeared to be of almost paper thinness and soft tissue technic was necessary to obtain films of diagnostic quality." Figures 1 and 2 show the knee joints in August 1933 and July 1934, respectively. Figures 3 and 4 show the tibias and fibulas in September 1933 and July 1934, respectively. Figure 5 shows the rarefaction and atrophy of the lower part of the thoracic and the lumbar portion of

Fig. 2.—Roentgenogram of the knee joints shown in figure 1 in July 1934.

the spine present in January 1934. The vertebrae are so thin in the center as to resemble biconcave lenses.

Creatine and Creatinine in the Urine.—Because of the muscular hypotonia and atrophy it was thought that examination of urine for creatine and creatinine might be of interest. Accordingly, weekly examinations of twenty-four hour specimens of urine were made for three months, and the results are given in the table. The most noticeable point is the variation in the daily output of both creatine and creatinine. This would lead to the suspicion that all the twenty-four hour specimens of urine were not being collected. As I was aware of this, every effort was made to insure complete collection, with, I think, success. It is also noticeable that the patient voided very small amounts in twenty-four hours. As the illness

progressed her intake of food and liquids grew smaller and smaller, until she subsisted on unbelievably little. Nine grams of amino-acetic acid was given at intervals as shown in the table. This appeared to have no effect on the amount of creatine or creatinine in the urine or on muscular hypotonia, but it did have a marked effect on the weight. When the administration of amino-acetic acid was stopped, a loss in weight followed, and when it was begun a gain in weight resulted. With the exception of the results of two determinations, the total creatinine coefficient was normal or above, excluding a progressive muscular atrophy. The values for the creatine in the urine were obtained by the method described by Folin and Wu [21] and those for creatinine by Folin's [22] procedure.

The ingestion of amino-acetic acid could not of itself be expected to increase the production of creatine in the urine as it has no guanidine radicle.

Effect of Administration of Vitamins A and D.—From Aug. 1, 1933, to Feb. 21, 1934, two hundred and five days, the daily average amount of vitamin A ingested was 18,546 units U. S. P. X, revised 1934 (13,247 U. S. P. X units), and

Data on the Amount of Creatine, Creatinine and Urea in the Urine of a Patient with Osteomalacia

Date, 1934	Specimens of 24 Hr. Urine, Volume in Cc.	Creatinine per 1,000 Cc. of Urine, Gm.	Creatine per 1,000 Cc. of Urine, Gm.	Patient's Weight, Kg.	Creatinine Coefficient	Creatine Coefficient	Total Creatinine Coefficient	Urea in 24 Hr. Specimens of Urine, Gm.	Amino-acetic Acid, 9 Gm. Daily
5/21	700	0.161	0.077	19.09	5.8	2.84	8.64	15.68	No
5/28	1,100	0.300	0.082	19.31	17.5	4.64	22.14	16.82	Yes
6/ 5	800	0.475	0.080	20.00	19.0	3.2	22.2	9.596	Yes
6/12	480	0.427	0.122	21.81	9.4	2.6	12.0	15.26	No
6/18	350	0.400	0.040	20.45	6.8	0.6	7.4	3.6	No
6/25	560	0.303	0.318	18.18	9.3	9.7	19.0	16.8	Yes
7/ 9	680	0.220	0.132	20.23	7.3	4.4	11.7	7.0	Yes
7/17	345	0.540	0.412	21.36	8.7	6.1	14.8	6.12	Yes
7/24	428	0.680	0.310	22.27	13.0	5.9	18.9	5.75	Yes
7/31	608	0.434	0.191	20.45	12.9	5.6	18.5	14.88	No
8/ 7	290	0.580	0.100	20.90	3.5	1.3	4.8	5.7	Yes
8/14	200	0.540	0.630	21.81	4.9	5.7	10.6	5.16	Yes
8/21	300	0.286	0.053	22.26	3.8	0.7	4.5	25.9	Yes

of vitamin D, 8,150 units U. S. P. X, revised 1934 (3,018 Steenbock units), as viosterol in halibut liver oil or fortified cod liver oil. From Feb. 21 to June 6, 1934, a total of one hundred and five days, the daily average amount of vitamin A ingested was 317,942 units U. S. P. X, revised 1934 (227,101 U. S. P. X units), and of vitamin D, 121,790 units U. S. P. X, revised 1934 (44,737 Steenbock units).

She was also at this time receiving ultraviolet therapy with a water-cooled quartz mercury vapor arc lamp three times weekly, fifteen minutes' (76 cm.) exposure at 30 inches general irradiation of the body and passive motion and massage three times weekly. On June 7, viosterol therapy was discontinued, as it was believed by this time to be of no value.

Progress Notes.—On March 19, a spontaneous fracture of the left femur occcurred at the junction of the middle and the lower third. A roentgenogram of the fractured femur on March 24 showed an advanced callus formation with apparently solid union. On August 29, a spontaneous fracture of the left tibia occurred

21. Folin, O., and Wu, H.: A System of Blood Analysis, J. Biol. Chem. **38**:381, 1919.

22. Folin, O.: On the Determination of Creatinine and Creatine in Urine. J. Biol. Chem. **17**:469, 1914.

Fig. 3.—Roentgenogram of the tibias and fibulas in September 1933.

Fig. 4.—Roentgenogram of the tibias and fibulas shown in figure 3 in July 1934.

with great pain. A posterior mold was applied. On September 4, the temperature started to rise, and the patient complained of severe pain in the left leg; she was nauseated and vomited. There was moderate edema of the left foot and leg. On the following day the patient complained of severe headache and abdominal pain. The temperature had risen to 101 F. On September 7 the patient complained again of severe abdominal pain with nausea and vomiting; the temperature rose

Fig. 5.—Rarefaction and atrophy of the lower part of the thoracic and the lumbar portion of the spine present in January 1934.

to 102.4 F. The blood count showed: hemoglobin, 74 per cent; white cells, 8,400; polymorphonuclears, 60 per cent; small lymphocytes, 20 per cent; red cells, 2,510,000. The urine contained a trace of albumin, acetone and amorphous urates. The temperature rose during the evening of September 8 to 104.4 F. The nausea continued, and blood was seen in the vomitus on macroscopic examination. The same evening the patient complained incessantly of abdominal pain. The next

morning the pulse became weak and thready. At 4 a. m. bright red blood was vomited and the abdomen became distended; the temperature dropped to 99.8 F. At 7 a. m. the patient became cyanosed, and oxygen was administered. The cyanosis became more marked and was totally unaffected by the oxygen; the patient died at 10:35 a. m.

Autopsy.—The significant gross findings at autopsy were as follows: fatty infiltration of the liver, hemorrhages in the mesenteric glands and absence of fat in the extremities with moderate muscular atrophy. Examination of the bones showed that the calvarium was thin, averaging approximately 2 mm. in thickness. The inner surface was corrugated by impressions of the convolutions of the hemispheres. It cut with ease and had a wide marrow space between the plates. The fossae at the base were normally developed, though of about the same consistency as the bones composing the vertex. The ribs were extremely fragile, being fractured by very slight pressure with the finger-tip. They likewise had a wide marrow space. The femur was easily sectioned and was largely composed of a peripheral shell.

Histologic examination of the tissues, made by Dr. C. V. Weller and Dr. S. C. Howard, failed to show any abnormalities of the glands of internal secretion. No evidence of a malignant process was found. The bones showed extreme osteoporosis without fibrosis or giant cell reaction. The epiphyses showed no imperfect or misplaced osteoid tissue. The cartilaginous zones and lines of ossification were of normal thickness and well defined.

SUMMARY

A case of generalized decalcification and atrophy of all bones in an 11 year old girl is described with laboratory findings and autopsy report. The picture is remarkably similar to that of the osteoporotic type of hyperparathyroidism without cystic degeneration described by Albright and his associates, but in the absence of demonstrable parathyroid disease at operation by a particularly qualified surgeon and at autopsy by a qualified pathologist, this diagnosis cannot be accepted. The osseous changes roentgenographically and histologically were not characteristic of juvenile or late rickets, and specific antirachitic therapy produced no improvement. The administration of amino-acetic acid by mouth produced a definite gain in weight, principally due to increased deposits of fat in the abdominal panniculus, but had no demonstrable effect on the creatine and creatinine in the urine or the muscular hypotonia. Criteria for differential diagnosis of diseases causing osteomalacic, osteoporotic and atrophic osseous changes are presented, and these conditions were ruled out as far as possible. It is concluded that the case presented is one of true juvenile osteomalacia the etiology of which remains to be discovered.

Dr. C. V. Weller, professor of pathology at the University of Michigan, and Dr. S. C. Howard, pathologist of St. Joseph's Mercy Hospital, Ann Arbor, Mich., assisted in the macroscopic and microscopic examination of the specimens in the case presented, and Dr. Angus Goetz and Dr. D. J. Hackett referred the patient to me.

Progress in Pediatrics

FATAL PAROXYSMAL VENTRICULAR TACHYCARDIA IN A YOUNG CHILD

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CHICAGO
AND
HARRY STRAUSS, M.D.
CLEVELAND

Sudden death as a result of uncomplicated paroxysmal ventricular tachycardia is uncommon. In only three of sixty-nine reported cases did the patient die during a paroxysm. It is highly probable that in these cases death was actually due to terminal ventricular fibrillation, a condition which may be so fleeting as to escape notice. Typical epileptiform seizures occurred in only three of the reported cases. We are reporting in this paper an unusual instance of paroxysmal ventricular tachycardia, starting at the age of 3, giving rise to frequent epileptiform attacks and finally to sudden death during a seizure. We had occasion to study the patient over a period of five years.

An unusual and carefully studied case was reported recently by Schwartz and Jezer. In describing the alterations in the rhythm of the heart preceding syncopal seizures of spontaneous ventricular fibrillation, the authors stated that these disturbances in rhythm present certain characteristics which are pathognomonic of the prefibrillatory stage. Essentially, the sequence of events as found in their case was: simple acceleration of the basic sinus rate, which was sooner or later disrupted by the interposition of premature ventricular beats with recurrent groups of aberrant ventricular complexes, many of which failed to be transmitted to the radial artery, producing a "pulse pause" and leading to a cessation of the apex beat. Loss of consciousness resulted when these periods lasted from twenty to forty seconds; longer periods were accompanied by convulsions. The patient died during an attack.

SURVEY OF THE LITERATURE

In a search of the literature we found reports of sixty-nine cases of proved paroxysmal ventricular tachycardia with sufficient data for

From the Sarah Morris Hospital for Children and the Heart Station, Michael Reese Hospital. Aided by the Frederick K. Babson Fund for study of diseases of the heart and circulation.

Data on Cases of Ventricular Tachycardia and Ventricular Fibrillation

Case	Author and Date	Sex	Age at Onset	Age at Death	Age at Time of Report if Living	Salient Points in History	Significant Physical Findings	Electrocardiographic Findings	Special Treatment	Autopsy	Comment
1	Hoffman 1911	F	18	..	23	Exertion induced tachycardia and vertigo	Regular pulse rate of 180 to 200 followed by irregular rhythm; pulse not palpable during attack	Regular ventricular rate of 180 followed by "delirium" of heart, succeeded by sinus tachycardia	.....	.....	Ventricular fibrillation, etiology: exertion (?)
2	Hart 1912	M	49	..	49	Palpitation; loud beating of heart at night; dizzy spells for 2 weeks prior to examination	Regular rate of 30 to 90 followed by extrasystoles and then a short phase of regular rate of 200; pulse not palpable during fast rate	Varying partial auriculoventricular block; bundle branch block; transient pulsus bigeminus and trigeminus; paroxysmal ventricular tachycardia, rate 240; retrograde conduction; electrical alternans	Digitalis produced a slowing of rate	.....	Etiology (?)
3	Butterfield and Hunt 1913	M	45	45	..	Admitted in state of congestive failure	Irregular pulse rate of 120 followed by regular rate of 150	Sinus rhythm; frequent ventricular extrasystoles; paroxysmal ventricular tachycardia with auriculoventricular dissociation	.....	Mural thrombus adherent to left side of intraventricular septum; septum replaced by vascular connective tissue	.....
4	Vaughan 1918	M	20	..	21	Recurrent spells of tachycardia and vertigo	Rheumatic heart disease; aortic and mitral insufficiency; pulsus alternans, bigeminus and trigeminus; periods in which regular rate was 180	Paroxysmal auricular tachycardia with pulsus bigeminus and trigeminus; periods of paroxysmal ventricular tachycardia; T wave negative in all leads	Pressure on eyeball aborted attacks by producing sino-auricular block	.....	Arrhythmia due to overdigitalization; return to sinus rhythm on stopping drug
5	Willius 1918	M	57	..	62	Exertion induced distressing palpitation and vertigo; 5 years' duration	.....	Pulsus bigeminus; paroxysmal ventricular tachycardia; impaired conduction rate 150	.....	.....	History of infection with streptococci
6	Idem	F	18	..	21	Sudden onset of tachycardia and palpitation with sudden cessation; 3 years' duration	.....	Paroxysmal ventricular tachycardia; rate 120, with intervening sinus rhythm	.....	.....	History of infection with streptococci
7	Idem	M	40	..	42	Tachycardia and palpitation; 2 years' duration	.....	Paroxysmal ventricular tachycardia	.....	.....	History of infection with streptococci
8	Idem	F	24	..	..	Tachycardia and palpitation; 6 weeks' duration	.....	Paroxysmal ventricular tachycardia; rate 125; arborization heart block	.....	.....	History of infection with streptococci
9	Idem	M	12	38	..	Tachycardia and palpitation; 26 years' duration	.....	Constant difference in appearance of lead 2; multiple ectopic	.....	Left coronary atheromatosis, myocarditis; areas of	Death by anemia

						6 weeks' duration		tachycardia; rate 125; arborization heart block			tion with streptococci
9	Idem	M	12	38	..	Tachycardia and palpitation; 26 years' duration	.....	Constant difference in appearance of lead 2; multiple ectopic impulses; rate 180	.....	Left coronary atheromatosis, myocarditis; areas of fibrosis in left ventricle; slight endocarditis of mitral and aortic valves	Death by anemia
10	Hume 1918	M	16	..	20	Onset of attacks of palpitation after diphtheria; free for 2 years; recurrence after 2 months in army	No evidence of cardiac disease	Paroxysmal ventricular tachycardia	Paroxysms stopped by assuming specific posture	.....	Etiology: diphtheria (?)
11	Idem	M	..	..	..	Exertion induced vertigo; palpitation periodically every 2 to 3 weeks for 21 months; duration of attack 2 hours	Excellent physical condition	Paroxysmal ventricular tachycardia	.....	.....	.....
12	Idem	M	..	..	..	Recurrent attacks of palpitation and precordial pain for 1 year	Excellent physical condition	Paroxysmal ventricular tachycardia	.....	.....	.....
13	Scott 1921	F	33	..	39	Recurrent attacks of vertigo during periods of rapid, irregular heart rate; duration 6 or 7 years	No evidence of cardiac disease; frequent extrasystoles; occasional regular rate of 150	Paroxysmal ventricular tachycardia; retrograde conduction	Studied effect of atropine, digitalis and epinephrine; quinidine, 2 grains daily, controlled attacks for 1 year of observation	.....	Exercise and excitement chief factors in inducing paroxysms
14	Robinson and Herrmann 1921	M	53	..	..	.....	.....	Paroxysmal ventricular tachycardía; coronary occlusion	.....	Infarction with gummatous lesion in circumflex branch of left coronary artery	.....
15	Idem	M	58	..	..	.....	.....	Paroxysmal ventricular tachycardia; coronary occlusion	.....	.....	.....
16	Idem	F	53	..	53	Paroxysmal attacks of tachycardia for 2 months	.....	Paroxysmal ventricular tachycardia with retrograde conduction every third beat	.....	.....	.....
17	Idem	M	49	..	..	Syphilitic and rheumatic; onset of tachycardia after coronary occlusion (?)	.....	Paroxysmal ventricular tachycardia with ventricular rate of 228 and auricular rate of 114	.....	.....	.....
18	Marvin and White 1922	F	21	..	21	Paroxysms of tachycardia and vertigo lasting from a few minutes to a few hours	No apparent cardiac disease	Paroxysmal ventricular tachycardia with ventricular rate of 262; auricular rate 131; paroxysmal ventricular tachycardia	.....	.....	Etiology unknown
19	Felberbaum 1923	F	54	..	54	Arrhythmia developed during overdigitalization	Hypertension; congestive failure	Paroxysmal ventricular tachycardia with extrasystoles alternating from 2 foci; rate of 140 to 180	.....	.....	Arrhythmia due to digitalis

Data on Cases of Ventricular Tachycardia and Ventricular Fibrillation—Continued

Case	Author and Date	Sex	Age at Onset	Age at Death	Age at Time of Report if Living	Salient Points in History	Significant Physical Findings	Electrocardiographic Findings	Special Treatment	Autopsy	Comment
20	Wolferth and McMillan 1923	F	20	..	20	Sudden onset of tachycardia and congestive failure	Heart enlarged; regular, rate 190; many extrasystoles; pulsus bigeminus	Paroxysmal ventricular tachycardia; auriculoventricular dissociation; auricular and ventricular extrasystoles	.....	.....	Recovery
21	Idem	M	61	61	..	.....	Advanced congestive failure; rate varied from 48 to 164	Auricular fibrillation; paroxysmal ventricular tachycardia; pulsus bigeminus	.....	No autopsy	.....
22	Idem	M	13	..	18	Recurrent failure since 13 years of age	.....	Auricular fibrillation; paroxysmal ventricular tachycardia; pulsus bigeminus	.....	No autopsy	.....
23	Idem	F	58	..	58	.....	Adenoma of thyroid gland and congestive failure	Auricular fibrillation; short runs of ventricular extrasystoles	Controlled by quinidine	.....	.....
24	Gallavardin and Berard 1924	F	55	..	56	Recurrent total block with pulse rate of 35 to 42 for 4 years with Stokes-Adams syndrome; in last year the seizures lasted up to 2½ minutes	.....	Ventricular fibrillation	.....	.....	True ventricular fibrillation (?)
25	Allan 1926	M	41	..	53	Recurring attacks of syncope and tremors of arms and face for 12 years	Heart rate too rapid to count during attack and pulse not palpable	Paroxysmal ventricular tachycardia with rate of 230 to 270; retrograde conduction and 2:1 block	Quinidine controlled rate	.....	No apparent cardiac disease
26	Jones and White 1926	M	5	..	18	Frequent attacks of tachycardia since 5 years of age; felt best when doing strenuous exercise	Heart markedly enlarged; rate 160; irregular	Paroxysmal ventricular tachycardia with ventricular rate 160 and auricular rate 95; normal rhythm after exercise with occasional ventricular extrasystoles	Quinidine 0.6 to 1.2 Gm. daily controlled rate	.....	No apparent etiology
27	Gilchrist 1926	F	52	52	..	Many attacks of rheumatic fever 20 years of age	Marked congestive failure; mitral and tricuspid incompetence; gallop rhythm; rate 150, regular	At first auricular flutter, then auricular fibrillation; ventricular tachycardia after massive doses of digitalis	.....	.....	Tachycardia was superimposed on a rheumatic cardiac condition and followed the use of massive doses of digitalis
28	Idem	M	62	64	..	Heavy drinker; precordial pain and dyspnea for 2 years	Congestive failure; auricular fibrillation	Paroxysmal ventricular tachycardia; rate 150	.....	.....	Etiology: alcoholism (?); ventricular tachycardia after large doses of digitalis
29	Idem	M	60	61	..	Convulsive seizures and unconsciousness on admission; similar attack 18 months previously; no cardiac	Sudden onset of tachycardia lasting 1 hour	Ventricular tachycardia; rate 200; evidences of myocardial exhaustion and coronary sclerosis	.....	.....	Etiology unknown, except for evidences of myocardial exhaustion and coronary sclerosis

29	Idem	M	60	61	..	Convulsive seizures and unconsciousness on admission; similar attack 18 months previously; no cardiac symptoms	Sudden onset of tachycardia lasting 1 hour	Ventricular tachycardia; rate 200; evidences of myocardial exhaustion and coronary sclerosis	.....	.....	Etiology unknown, except for evidences of myocardial exhaustion and coronary sclerosis
30	Idem	M	40	..	41	Short attacks of giddiness and dyspnea for 1 year; heavy smoker	Heart slightly enlarged to left; pulse irregular	Ventricular tachycardia; ventricular rate 150 and auricular rate 107	Reduced consumption of tobacco	.....	Tachycardia did not recur after consumption of tobacco was reduced; etiology: nicotine intoxication (?)
31	Idem	M	17	..	19	Transient attacks of giddiness and palpitation with abrupt cessation	Irregular rate	Ventricular paroxysms mixed with multiple extrasystoles and beats of normal origin	Stooping forward stopped paroxysms; digitalis had no effect; quinidine, 7 grains daily, controlled attacks	.....	.....
32	Major and Wahl 1926	M	12	25	..	Two paroxysms of tachycardia since 12 years of age; dental caries for 18 months prior to death; two attacks a few months after extraction of teeth and a third shortly before death	No evidence of cardiac disease	Right ventricle preponderating Q R S slurred on all leads; T_1 negative; paroxysmal ventricular tachycardia	Morphine given for relief of attacks	Acute and chronic focal myocarditis; aortic intimitis; early coronary arteritis; chronic pericarditis	Definite relation
33	Palmer and White 1927	M	50	50	..	Arrhythmia developed after coronary occlusion	Hypertensive cardiac disease	Paroxysmal ventricular tachycardia with bidirectional alteration in complexes	.....	Recent thrombus in left branch of coronary artery; infarct at apex of left ventricle	.....
34	Idem	M	45	..	45	Recurrent congestive failure	Auricular fibrillation	Paroxysmal ventricular tachycardia	.....	.....	Arrhythmia developed during digitalization
35	Moore 1928	M	11	..	17	Recurrent attacks of tachycardia and dyspnea since 11 years of age; congestive failure at 12; quinidine taken for 56 months after that; attacks became infrequent, and patient able to carry on light exercise	No evidence of cardiac disease	Paroxysmal ventricular tachycardia	Quinidine seemed to control attacks	.....	No apparent etiology
36	Gallavardin and Veil 1929	M	16	..	17	Incapacitated for 18 months because of frequent attacks of vertigo and palpitation	No apparent cardiac disease; pulse disappeared during paroxysms	Frequent "salvos" of ventricular extrasystoles; also long runs at rate of 228	.....	....	Etiology unknown
37	Levine and Fulton 1929	F	32	..	42	Palpitation, dyspnea, cough, pain in chest at intervals since influenza at 32 years of age; diphtheria at 7 years; no history of rheumatic disease	Runs of rapid regular beats alternating with periods of normal rhythm; occasional extrasystoles	Ventricular tachycardia	Quinidine used with remarkable results	.....	.....

Data on Cases of Ventricular Tachycardia and Ventricular Fibrillation—Continued

Case	Author and Date	Sex	Age at Onset	Age at Death	Age at Time of Report If Living	Salient Points in History	Significant Physical Findings	Electrocardiographic Findings	Special Treatment	Autopsy	Comment
38	Idem	M	21	..	48	Occasional dyspnea and cough; one severe attack of "heart fluttering;" died of intercurrent lobar pneumonia	Slightly dyspneic; auricular fibrillation; rate 150	Auricular fibrillation; ventricular tachycardia, rate 183	Digitalis had no effect; quinidine 0.8 Gm. three times a day restored sinus rhythm, rate 73	Lobar pneumonia; mitral stenosis	.....
39	Idem	M	61	..	64	Mild diabetes; a severe attack of constricting substernal pain	Occasional attacks of irregular heart action, rate 150, following attack of coronary thrombosis	Ventricular tachycardia	Quinidine had no effect because administration of it was started late and in insufficient amounts	.....	.....
40	Idem	M	51	51	..	Dyspnea for 3 months	Congestive failure with pericardial rub and rapid regular rhythm	Ventricular tachycardia, rate 153; defective intraventricular condition	Quinidine controlled attack	Coronary occlusion with infarct in wall of left ventricle	Quinidine controlled tachycardia; death due to coronary occlusion
41	Idem	M	56	56	..	Sudden attack of severe substernal pain with absence of pulse; revived by epinephrine	Blood pressure 84/50; apex rate 104 slowed to normal; later sudden tachycardia, rate 171, regular	.....	Quinidine controlled attack	None	Sudden death after apparent improvement; coronary thrombosis
42	Idem	M	61	61	..	Dyspnea for few months, with substernal pressure on exertion; one sudden attack of collapse, violence and delirium	Apex rate 204; tones distant with short pauses	None	Quinidine controlled tachycardia	None	Coronary thrombosis; sudden death from cerebral accident
43	Idem	M	53	..	53	Severe precordial pain, 3 hours' duration	Blood pressure 158/110; gallop rhythm, rate 124; sudden attack of rate 198	Ventricular tachycardia	Quinidine 1.5 Gm. 5 times daily restored normal rhythm, which became permanent	.....	Coronary thrombosis
44	Idem	M	54	55	..	Hypertension; dyspnea for 1 year; sudden substernal pain	Coronary thrombosis; attack of tachycardia with thready pulse	Paroxysmal ventricular tachycardia	Quinidine controlled tachycardia	Complete occlusion of left coronary artery	Quinidine controlled tachycardia; death due to rupture of heart
45	Idem	M	55	..	55	Sudden onset of substernal pain; tachycardia	Rate 160; sound feeble; slightly irregular and varying in intensity	None	Quinidine produced abrupt cessation of tachycardia	.....	Ventricular tachycardia diagnosed on characteristic findings superimposed on an obvious coronary thrombosis and on response to treatment with quinidine
46	Idem	F	50	..	..	Sudden substernal pain 9 days previous to examination	Rate 180; sounds of varying intensity	Ventricular tachycardia; complete auriculoventricular dissociation	Quinidine failed to slow the rate	.....	*Only case in ten reported by the authors in which treatment with quinidine failed to produce response*
47	Goodman and DeGraff 1929	F	13	..	..	Pressure on precordium produced tachycardia which ceased on release	Mitral stenosis; active rheumatic carditis	Auriculoventricular dissociation with auricular rate 80 and ventricular rate 170	.....	.....	Stimulus was a direct effect of pressure and not a cutaneous phe-

						ous to examination		tricular dissociation			authors in which treatment with quinidine failed to produce response
47	Goodman and DeGraff 1929	F	13	..	..	Pressure on precordium produced tachycardia which ceased on release of pressure	Mitral stenosis; active rheumatic carditis	Auriculoventricular dissociation with auricular rate 80 and ventricular rate 170	.....	.....	Stimulus was a direct effect of pressure and not a cutaneous phenomenon; vagal stimulation inhibited this effect; sympathetic stimulation with vagus paralyzed tended to produce arrhythmia
48	Barker 1930	M	20	..	..	Recurring attacks of unconsciousness, cyanosis and tachycardia	Slight cyanosis; liver enlarged; pulse 81 with occasional extrasystoles	Rate 67; ventricular extrasystoles from multiple foci; P_1 and P_2 notched; intraventricular block; deviation of right axis	.....	.....	No electrocardiogram during paroxysm
49	Schwam 1931	M	47	53	..	Several attacks of congestive failure; taking digitalis	Stupor; pulse not palpable; blood pressure could not be taken; apex rate 200	Ventricular tachycardia, rate 220; later auricular fibrillation; complete heart block; idioventricular rhythm	Quinidine controlled attacks for several weeks	Moderate change in myocardium, coronary arteries and aorta	Attacks followed intoxication due to digitalis
50	Idem	M	54	55	..	Dyspnea, swelling of feet and precordial pain for 7 months	Irregular pulse; extrasystoles; pulsus bigeminus	Ventricular tachycardia, rate 160	Quinidine controlled attacks	.....	Followed intoxication due to digitalis; death in uremic coma
51	Idem	M	65	..	65	Dyspnea and swelling of feet for 2 weeks; gonorrhea 20 years ago but no chancre	Congestive failure; double aortic valvular defect premature beats	Alternating bidirectional ventricular tachycardia	Quinidine produced cessation of ventricular paroxysms	.....	Paroxysms followed prolonged use of digitalis
52	Strauss 1930	M	49	49	..	Tachycardia developed during digitalization	Syphilitic cardiac disease; slight failure; aortitis	Auricular fibrillation; paroxysmal ventricular tachycardia with bidirectional alternation of the complexes	Controlled by quinidine	Adherent pericardium; syphilitic aortitis	.....
53	Idem	M	73	..	..	.....	Congestive failure	Paroxysmal ventricular tachycardia during digitalization	Cleared up on treatment with quinidine	.....	Death
54	Anderson 1931	M	17	..	20	Paroxysmal attacks of rapid, irregular heart beat with vertigo palpitation and one period of syncope, over a period of 3 years; came on with exertion and excitement	No evidence of cardiac disease; rapid, irregular beat	Auriculoventricular dissociation; paroxysmal ventricular tachycardia; rate 220, with retrograde conduction	Quinidine, 5 grains 2 times a day controlled paroxysms	.....	Etiology unknown
55	Wilson, et al. 1932	M	23	31	..	Attacks of dyspnea; tachycardia for 8 years; occasionally accompanied by unconsciousness	Occasional extrasystoles	Pulsus bigeminus due to ventricular extrasystoles; after exercise ventricular tachycardia developed with rate of 200 to 243	Quinidine had favorable effect	.....	Sudden death after a period of improvement; attacks could be induced at will by exertion

Data on Cases of Ventricular Tachycardia and Ventricular Fibrillation—Continued

Case	Author and Date	Sex	Age at Onset	Age at Death	Age at Time of Report if Living	Salient Points in History	Significant Physical Findings	Electrocardiographic Findings	Special Treatment	Autopsy	Comment
56	Idem	M	50	..	52	Dyspnea, palpitation brought on by exertion; 2 years' duration	None	Normal when at rest; ventricular tachycardia induced by exertion; rate 168 to 188	Quinidine produced favorable effect	.....	Attacks brought on by exertion
57	Idem	F	30	..	30	Palpitation for several years	None	Normal at rest; exertion produced many ventricular extrasystoles	Quinidine lessened but did not abolish extrasystoles	.....	Attacks brought on by exertion
58	Idem	M	22	..	25	Palpitation for 3 years	Cardiac arrhythmia	Numerous ventricular extrasystoles	None	.....	.....
59	Bellet and MacMillan 1931	F	16 (?)	..	17	Tachycardia incidental finding in routine examination during pregnancy; cesarean section with no complications, tachycardia present 1 year later	Rapid, irregular heart rate	Almost continuous paroxysms of ventricular extrasystoles; occasional pulsus bigeminus; T_2 and T_3 inverted; auriculoventricular dissociation	Digitalis tried; quinidine controlled arrhythmia	.....	No evidence of cardiac disease other than arrhythmia; etiology unknown
60	Coelho 1932	M	30	30	..	Attacks of vertigo and syncope as often as 60 times a night prior to admission	Pulse regular; rate 27; not palpable during long runs of extrasystoles lasting 50 seconds	Auriculoventricular dissociation with complete and incomplete block; runs of ventricular extrasystoles for 50 seconds with unconsciousness	.....	.....	Died during attack
61	Hollingsworth 1932	M	39	39	..	Diabetes; sudden onset of tachycardia, dyspnea and congestive failure; recurrences of paroxysmal tachycardia lasting from 20 minutes to 13 days	Congestive failure; pulse rapid, regular, rate of 150 to 190	Ventricular tachycardia, rate 214; ventricular extrasystoles from multiple foci; changes indicating coronary occlusion	Pressure on ocular vagus nerve had no effect; quinidine stopped some paroxysms	Occlusion of left descending branch of coronary artery; anterior infarct pericardial and diaphragmatic adhesions	Paroxysmal ventricular tachycardia following coronary occlusion
62	Bunn 1933	M	52	..	54	Neurasthenic make-up; onset of hyperthyroidism 3 months before thyroidectomy; tachycardia developed 3 hours after operation and lasted 48 hours; left hospital with normal rhythm	No evidence of organic cardiac disease	Normal electrocardiogram 1 year before operation; paroxysmal ventricular tachycardia, rate 300; following administration of quinidine this changed to auricular fibrillation and then to sinus rhythm	Digitalis; quinidine	.....	Electrocardiogram not absolutely positive for paroxysmal ventricular tachycardia

with normal rhythm

63	Clerc, Levy and Zodoc-Kahn 1933	M	53	56	..	Attacks of palpitation for 3 years; prior to observation almost continuous attacks	Normal rhythm interrupted by long runs of rapid beats with sudden onset and cessation; pulse faint in these periods	Sinus rhythm; paroxysmal ventricular tachycardia, rate 220	.....	.....	Organic cardiac disease (?)
64	Howard 1933	M	..	..	..	Rheumatic cardiac disease; recurrent congestive failure; digitalis for 2 years	Auricular fibrillation; congestive failure	Auricular fibrillation interrupted by runs of bidirectional ventricular extrasystoles	Digitalis	.....	Ventricular tachycardia cleared up when medication was discontinued
65	MacKinnon 1934	M	24	29	..	Sudden onset, while playing football, of pain in chest and tachycardia; persisted intermittently for 5 years; congestive failure developed and patient died	Not given	Paroxysmal ventricular tachycardia with alternation in shape and time of complexes; rate 132; occasional pulsus bigeminus	Digitalis; quinidine	Dilatation and hypertrophy of heart	Etiology unknown
66	Schwartz and Jezer 1934	M	17	17	..	Recurrent syncopal attacks and epileptiform convulsions	Infectious myelitis; heart rate 92; regular; between attacks; heart sounds not heard and pulse not palpable during seizures lasting 35 to 90 seconds	Sinus rhythm between attacks; transient ventricular fibrillation during seizures; rate about 300	.....	.....	Death during a paroxysm
67	Schwartz and Hauswirth 1934	F	56	57	..	Recurrent attacks of syncope and convulsions with loss of sphincter control	Hypertension; normal sinus rhythm between attacks	Sinus rhythm alternating with auriculoventricular dissociation; pulsus bigeminus, trigeminus and quadrigeminus; transient ventricular fibrillation	.....	.....	Transient ventricular fibrillation
68	Strong 1934	F	53	53	..	Adams-Stokes syndrome for 16 months; sudden onset of tachycardia with convulsions 16 hours before death	Apex rate varied from 36 to an extremely rapid rate	Complete auriculoventricular block; auricular rate 90, ventricular rate 35; paroxysmal ventricular tachycardia	Quinidine had slight effect	.....	.....
69	Elliott and Fenn 1934	F	18	19	..	Two years prior to illness had lost 70 pounds in 4 months by dieting; dyspnea, nausea and vomiting and paroxysmal tachycardia developed during attempt to lose weight again	Severe congestive failure; apex rate 170 to 210 continuously for 18 days	Paroxysmal ventricular tachycardia; complete auriculoventricular dissociation; ventricular rate 174, auricular rate 90; retrograde conduction	Digitalis had no effect; quinidine controlled paroxysms for a time	.....	Congestive failure and death occurred following attack of paroxysmal ventricular tachycardia lasting 32 days; severe dieting may have been factor in producing arrhythmia

analysis. A study of these reports (table 1) brought out a number of interesting facts, of which the following are the more important:

Age at Onset.—The youngest patient proved to have ventricular tachycardia was a boy in whom the symptoms began at the age of 5 years (case 26, Jones and White). The largest group of cases, twenty-two, occurred in the sixth decade. The next largest, fourteen, occurred in the second decade. Eleven cases were reported which occurred in the fifth decade, eight in the third, six in the fourth, five in the seventh and two in the eighth. Our patient, in whom the symptoms began at the age of three years, is, so far as we know, the youngest whose case is on record.

Etiology.—No definite inferences can be drawn from the literature as to the possible etiologic factors specifically concerned with the production of this form of arrhythmia. About one third of the patients presented definite evidence of rheumatic and coronary disease. In ten of the cases, intoxication due to digitalis was definitely the cause, and the condition disappeared on discontinuance of the drug. Others had a history of a recent infection with streptococci (cases 5, 6, 7 and 8). Diphtheria and badly infected teeth seemed to be the plausible factor in two other cases. Nicotine, alcoholism and neurasthenia were mentioned as possible factors in other cases. Exertion seemed to be the exciting cause of paroxysms in many patients in whom no other abnormality could be found. In fourteen cases there was no demonstrable exciting cause.

Symptoms and Physical Findings.—Subjectively, the most common symptoms were recurrent attacks of palpitation, dyspnea, dizziness and faintness. In only three cases were typical epileptiform seizures described (cases 25, 29 and 66). In a fairly large number of cases the radial pulse was absent during the seizure. The fastest heart rate recorded was 300 per minute (cases 69 and 66). In the cases in which organic cardiac disease was present, findings of congestive failure and coronary disease predominated.

Pathology.—Twelve autopsy reports were recorded. The lesions were predominantly the same as those seen in cases in which death was due primarily to myocardial or coronary disease. No mention was made of any abnormalities in the conductive system. There was no hint in the reports of any specific organic basis for the arrhythmia.

Course and Prognosis.—At the time when the cases were reported, thirty-four of the patients were alive and twenty-four were dead. The status of the other patients at the time when the cases were reported was not clearly stated. The longest duration of symptoms was twenty-six years (case 9), and the patient died by suicide. By far the largest number of patients dated the onset of symptoms as less than five years

previous to the time when the case was brought to the attention of the physician. Only three patients died during a paroxysm (cases 55, 60 and 66). Most of the deaths were due to the associated disease, chiefly congestive failure and coronary accidents.

Treatment.—The paroxysm itself was occasionally aborted by such a simple measure as pressure on the eyeball or carotid sinus or the assumption of specific postures. The drug therapy centered around the use of quinidine. Levine and Fulton used this substance in ten cases of paroxysmal ventricular tachycardia, and in nine of them the action was practicaly specific (cases 37 to 46). Twenty-six patients are reported in whom the condition was improved or cured by the use of quinidine salts. Schwartz and Jezer, however, gave warning that this drug may precipitate attacks of ventricular fibrillation in cases in which the prefibrillatory mechanism is present.

REPORT OF A CASE

History and Course.—F. M., a girl aged 8 years, was under our observation in the Mandel Clinic of the Michael Reese Hospital from the age of 14 months. Her mother had recently died, and the child had been placed in a foster home. Her father and four sisters were living and well. The early developmental history was entirely normal. At the age of 16 months the child was reported as being very pale and having large, cryptic tonsils.

She had repeated sore throat prior to tonsillectomy, at the age of 3 years, pertussis at the age of 6 years and German measles at 7 years. She had epidemic parotitis and an infection of the upper respiratory tract while in the hospital. On June 26, 1929, when she was 3 years old, the child was seen by Dr. Rubell, and the following history was given by the foster mother: Three weeks previously the child, while playing, suddenly gasped for breath, fainted and "looked dead" for about two minutes. The attack was not accompanied by frothing at the mouth or biting of the tongue, and there was no injury from the fall. After regaining consciousness the child seemed weak and fell into a deep sleep. A similar attack occurred two weeks later. Examination at that time revealed a rather pale child, otherwise normal. A diagnosis of idiopathic epilepsy was made, and the child was put on a ketogenic diet and given small doses of phenobarbital. The diagnosis was corroborated by several competent neurologists.

A third attack occurred ten months later, on April 5, 1930. This resembled the previous ones but was accompanied by some twitching of the muscles. After that the seizures recurred at intervals varying from a few days to several months. Some attacks consisted merely of sudden momentary pallor and blueness of the lips, without coma. These we interpreted at the time as epileptic equivalents. The seizures usually occurred during play, or on the way to or from school.

Our suspicion of the true nature of the attacks was aroused on April 13, 1932, two days after an attack, when the cadiac rate during a routine examination was found to be 180 per minute and two minutes later it suddenly slowed down to 72 per minute. There were no subjective symptoms either during the period of tachycardia or during the sudden transition to the slower rate. Careful observation of the pulse during the succeeding months revealed irregularly alternating periods of bradycardia and tachycardia, the pulse rate ranging from 46 to 180 or faster.

Early in 1933 the foster mother, to whom the child had been very much attached, suddenly died. Following this emotional upset, the attacks of unconsciousness became more frequent, and the child was sent to the hospital.

At the hospital the following observations were made: The seizures were brought on chiefly by psychic stimuli. On one occasion a severe attack was precipitated by merely asking her to come to another room to be weighed. The child later explained that she thought she was going to be hurt. A typical seizure observed in the hospital occurred as follows: There was apparently a strong premonition of an impending attack, because the child screamed and reached for support. The pulse became too rapid to count. Coma developed quickly, accompanied by irregular convulsive movements. The patient became pale during the period of coma; no heart tones were audible at the apex, and the radial pulse disappeared. The longest "pulse pause" observed was fifty seconds. Gradually the heart tones returned. At first these were very rapid and faint, but they gradually became more and more audible. The pulse at the wrist then reappeared. It was rapid and thready at first, but it gradually increased in volume and slowed. The pallor was replaced by flushing. Retching but no vomiting followed the attack. As the patient regained consciousness she felt apathetic and tired and fell into a deep sleep.

During the intervals between seizures the child was playful, enjoyed talking about her condition with other children and apparently could bring on a "spell"

Fig. 1.—Electrocardiogram (two beats each from leads I, II and III) taken during a period of clinical quiescence: average pulse rate 75, PR interval 0.14 second, QRS complex slurred, Q_3 present, T_3 inverted and small, P_1 notched and P_3 usually inverted. The P wave changes in contour from beat to beat in all leads. The interpretation was: Sinus arrhythmia with shifting pacemaker.

at will. The pulse, although regular most of the time, occasionally revealed frequent extrasystoles, especially soon after one of her seizures.

On April 4, 1934, a typical seizure came on without warning, and she did not recover. Artificial respiration and cardiac stimulants which were used were of no avail.

Laboratory Data.—The hemoglobin content varied between 67 per cent and 80 per cent (Sahli). The red blood cell count varied from 3,000,000 to 4,000,000. The white blood cell count and the differential count were normal. The urine was normal. The calcium content of the blood was 12.7 mg. per hundred cubic centimeters, the nonprotein nitrogen content 35 mg. and the cholesterol content 240 mg.

Roentgen examination showed the sella turcica to be normal. The convolutional markings of the brain were increased. There was no evidence of a neoplasm of the brain. The diameter of the heart was 9.5 cm., and the diameter of the chest was 18.5 cm., indicating a slightly increased cardiac width. There was no definite accentuation of the pulmonic bow. The reaction to the test for dextrose tolerance was normal. The spinal fluid was normal. The reaction to the Mantoux test with a dilution of 1:1,000 was negative.

Electrocardiograms.—A large number of tracings were taken, the following being typical of the entire series. A tracing taken during a period of clinical quiescence (fig. 1) shows an average rate of 75 and a P-R interval of 0.14 second. There is slurring of the QRS complex; Q_1 is present, T_3 is inverted and small, P_1 is notched and P_3 is usually inverted. The P wave changes in contour from beat to beat in all leads. The interpretation was sinus arrhythmia with shifting pacemaker. The changes suggest myocardial damage at this age. The shifting pacemaker is more clearly shown in figure 2.

On several occasions a sino-auricular block was noted, as shown by sudden halving of the rate, as in figure 3, from 106 to 53 per minute. This might explain some of the sudden changes in rate which were observed. For some time after the attacks pulsus bigeminus developed on the slightest movement or psychic suggestion. As figure 4 shows, the second beat of the pulsus bigeminus was an auricular extrasystole, as indicated by the premature abnormal P wave. The conduction through the ventricle of these beats was aberrant, explaining the bizarre

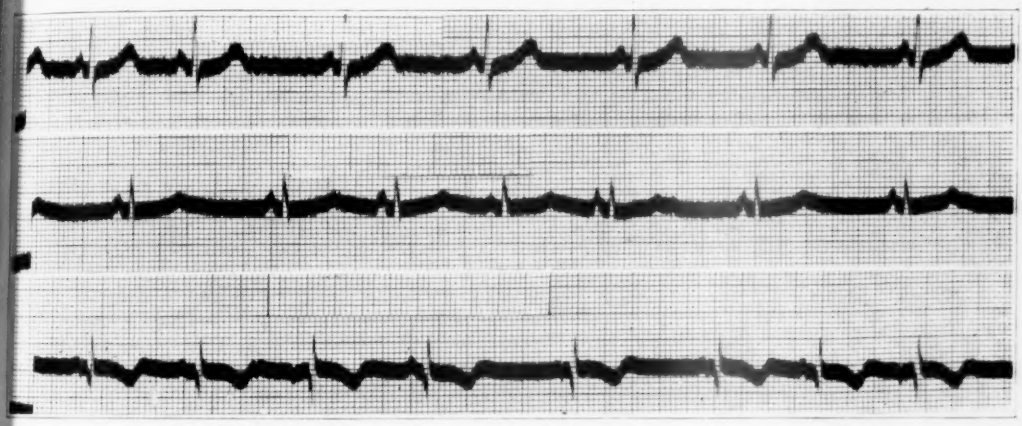

Fig. 2.—Electrocardiogram taken during a period of clinical quiescence. Average pulse rate 68. The shifting pacemaker is shown more clearly than in figure 1.

character of the ventricular complex as compared with the normal. Perhaps some instances of sudden slowing of the pulse noted in this patient were caused by the failure of such extrasystoles to reach the radial artery.

Because twitchings of the muscles always accompanied the seizures, no records were obtained during attacks, but a number of records were obtained just before (fig. 5) or within a minute or so after such seizures (fig. 6). It was noted that the heart was in a sort of "delirium," in that the rate varied from 250 to 300 beats per minute and the mechanism was a typical paroxysmal ventricular tachycardia, the beats originating from multiple pacemakers with some supraventricular conducted beats probably interspersed. While figure 5 was being taken an attack with convulsions developed, during which the lead was kicked off. In figure 6 *A* the rapid undulations shown are extracardiac and due to muscle tremors, the result of minor convulsive seizures. Figure 6 *B*, taken a few minutes afterward, shows the persistence of the tachycardia while the patient was improving clinically.

Excerpts from Autopsy Report.—External Examination: Autopsy was performed one hour post mortem. The body was that of a well developed and well nourished girl about 10 years of age.

Internal Examination: The skin on section was elastic. The subcutaneous fat tissue was abundant throughout, measuring 14 mm. in the midline.

The serous cavities were smooth, moist and glistening throughout. The bronchial and mesenteric lymph nodes were enlarged, soft and gray-brown.

The heart weighed 175 Gm. It was large but of normal shape. The pericardium was smooth, gray and shiny. The myocardium was firm and deep red and measured 1.3 cm. at the base of the left side of the heart. The chordae tendineae and the columnae carneae were thickened and prominent. The endocardium was smooth and glistening. The valvular apparatus was intact. The coronary arteries were patent. The intima of the coronary arteries and aorta was smooth and shiny.

The left lung weighed 140 Gm. and the right 160 Gm. The external surfaces were reddish gray and smooth. The lungs were crepitant throughout, and on section the surfaces were deep red and smooth and exuded a moderate quantity of a markedly hemorrhagic frothy material. The trachea and bronchi presented no changes.

The liver weighed 750 Gm. and was of normal size and shape. The capsular surface was smooth and shiny and gray over the deeper reddish-blue surface of the liver. On section the central zones were indistinct and surrounded by rather prominent periportal spaces.

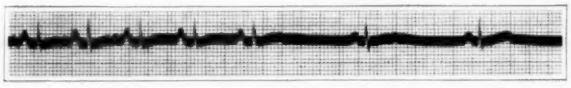

Fig. 3.—A sino-auricular block shown by the sudden halving of the pulse rate from 106 to 53 beats per minute (lead II).

The spleen was enlarged and soft and weighed 100 Gm. On section, the surfaces were dull gray for the most part, with only moderate blue markings between.

The kidneys together weighed 275 Gm. and were of firm consistency. On section, the capsule stripped readily, revealing a smooth surface. The sectioned surfaces were deep red, with normal architectural markings. The pelves, ureters and bladder showed no changes.

The pancreas and adrenals presented no noteworthy macroscopic changes.

The mucosa of the stomach and duodenum and the first portion of the large intestine were studded by small, raised gray-brown areas, the centers of which were marked by minute black dots.

The brain was removed and was seen to be enlarged, soft and edematous. After fixation in solution of formaldehyde the gyri appeared flattened. The sulci could hardly be made out. The subarachnoid vessels were markedly hyperemic, causing a more or less purplish discoloration of the cortical portions of the brain. Multiple sections throughout the brain revealed many dilated blood vessels and an occasional area of petechial hemorrhage. There was no evidence of tumor or abscess in the brain. Sections cut through various portions of the brain were embedded in paraffin.

Microscopic Examination: Sections of the brain revealed marked hyperemia of the blood vessels. In the region of the basal nuclei the ganglion cells were larger than normal. The cytoplasm was swollen and distinctly granular. In many instances the nuclei could not be made out. There were no cellular infiltra-

tions in any of the sections examined. There was no increase in glial tissue. Several sections, particularly the ones which were taken from the walls of the third and fourth ventricles, revealed free red cells outside the wall of the fourth ventricle. The petechial hemorrhages showed no evidence of organization. No old blood pigment was found in any of the sections. The meninges showed no changes. The subarachnoid vessels were markedly dilated and filled with red cells. The ependymal lining was intact throughout.

The routine sections of the heart revealed that the muscle fibers were slightly swollen, but the striations in many portions could be made out clearly. In the region of the bundle of His the intercalated disks were prominent. The sections taken from the anterior wall of the left ventricle also revealed prominent disks.

Sections were also taken from the region of the auriculoventricular node, from the sinus node, from various portions of both auricles and from the septum in

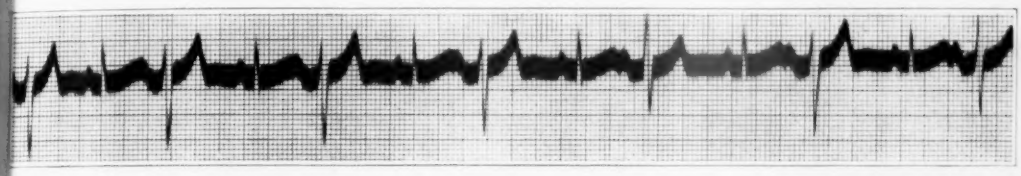

Fig. 4.—Pulsus bigeminus; the second beat is an auricular extrasystole shown by premature abnormal P waves (lead II).

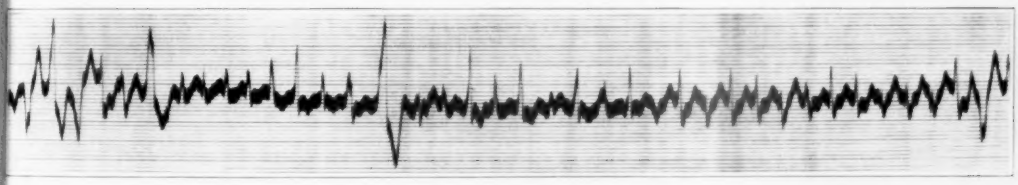

Fig. 5.—Electrocardiogram taken just before a seizure (lead II).

the region of the bundle of His. These sections were stained with hematoxylin and eosin, with iron hematoxylin and according to the Van Gieson method. Other stains were also used when deemed necessary.

Sections taken from these regions showed various changes: In the auriculoventricular node a few areas were noted which revealed a distinct but slight increase of connective tissue. It seemed that the connective tissue sheaths of the anterior bundle of His were thicker than normal. Very occasionally, lymphocytes and endothelial cells were seen within the sheaths of the bundle. Sections from the interventricular septum itself also revealed an increase of connective tissue. The bundle of His seemed thinner than normal, and its striations were partly obscured. The intercalated disks, however, as was mentioned before, were very clearly noted. Sections taken from the sinus node revealed a marked new formation of connective tissue. In some portions large areas of muscle fibers were replaced by connective tissue, and the Van Gieson stain revealed only an occasional islet of yellow-stained fibers in the midst of the connective tissue. The endocardial surface of the region of the sinus node also revealed an increase of

connective tissue. One section, which was taken from the wall of the inferior vena cava, revealed, in addition to newly formed fibers of connective tissue, a considerable number of lymphocytes, endothelial cells and a very occasional polymorphonuclear leukocyte. The lymphocytes, however, predominated. Also, sections taken from other portions of the auricle revealed inflammatory cells, which in several instances were arranged in groups and which were distinctly subendocardial in location. The predominating type of cell in this region was the lymphocyte. Sections from the papillary muscles revealed a marked new formation of connective tissue, which was found not only in the tips of the muscle but also extending throughout its body. Sections from the septal surface of the right auricle revealed distinct perivascular fibrosis. In only a few fields it was seen that the newly formed fibers of connective tissue encircled small groups of muscles entirely.

Fig. 6.——Electrocardiogram taken immediately after a seizure, showing "delirium" of the heart with a heart rate of 250 to 300 (lead II).

Careful examination of the blood vessels in all the sections taken from the myocardium revealed no evidence of histopathologic lesions.

Comment: The outstanding changes in these sections were those in the heart. There was marked fibrosis, possibly most pronounced in the right auricle. Portions of the septum and papillary muscles of the left ventricle were also distinctly involved. Occasionally inflammatory cells were seen within the fibrotic area, lymphocytes being the predominating type. The presence of inflammatory cells, though not marked, probably revealed the pathogenesis of the fibrotic lesions, as being the result of primary inflammatory changes. While the presence of lymphocytes at first glance might suggest syphilis as the cause of the changes, the absence of changes of the blood vessels and other characteristics of syphilis makes it seem unlikely that syphilis was the cause of the fibrosis. It seems plaus-

ible that the child had suffered from an infectious disease (scarlet fever, diphtheria, or an infection of the upper respiratory tract of nonspecific nature). The myocardium at that time apparently showed acute inflammatory changes which had healed, resulting in the scars in various places (fibrosis).

There was no evidence of a tumor or any other lesion in the brain, which might be responsible for epilepsy. All changes found in the brain, namely, the marked hyperemia and the petechial hemorrhages, were recent. Whether the hemorrhages which were found in the walls of the third and fourth ventricles were responsible for the more or less sudden death of this patient cannot be definitely decided.

Pathologic Diagnosis: Included in the pathologic diagnosis were: fibrosis of the myocardium, particularly involving the right auricle, sinus node, auriculoventricular node and bundle of His (probably the result of a primary myocarditis); dilatation of the heart; marked edema of the brain, with petechial hemorrhages; cloudy swelling of the liver; edema of the lungs; passive hyperemia of the lungs

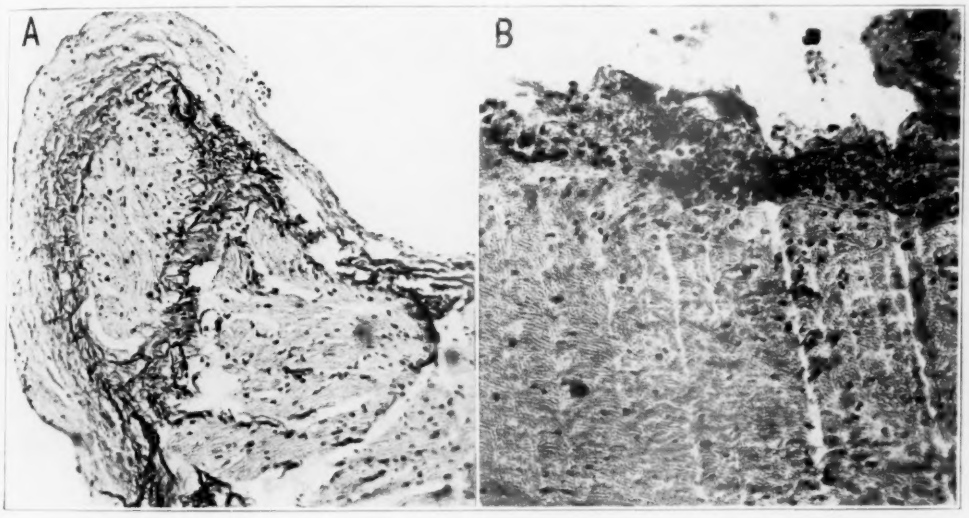

Fig. 7.—*A*, section from the right auricle, showing marked fibrosis (Van Gieson's stain). *B*, section from the right auricle, showing infiltration by lymphocytes (hematoxylin-eosin stain).

and kidneys; follicular hyperplasia of the stomach, duodenum, large intestine and spleen, and enlargement of the thymus gland and lymph nodes.

COMMENT

The clinical course and electrocardiographic records revealed an extraordinarily irritable heart, with sudden and extreme changes in rate often initiated by mere psychic stimuli, with the presence of transient arrhythmias and culminating in a so-called "delirium" of the ventricle with multiple foci of discharge and a rate of 300 per minute just preceding the onset of coma and convulsions. These changes closely resemble those described by Schwartz and Jezer as pathognomonic of the

prefibrillatory stage of transient ventricular fibrillation. Unfortunately, because of the severity of the convulsions, we were unable to obtain a tracing during the actual "pulse pause." By analogy, however, one may assume that in this case the ventricles were probably in a state of actual fibrillation during the period of coma and convulsions and that it was this that accounted for the fatal outcome. It is possible, however, that the tachycardia itself could have caused the attacks without invoking ventricular fibrillation except in the fatal attack.

Death was probably the result of anoxemia of the brain and myocardium during the period of fibrillation. Whether the pathologic changes in the conduction system in our case were the cause or the result of the repeated seizures cannot be definitely determined. Clinically it would seem that the tachycardia was primarily on a psychoneurotic basis and that the repeated periods of anoxemia so induced resulted in the fibrotic changes of the myocardium. The evidences of inflammation may have been secondary to a minor infection or to the anoxemia itself.

SUMMARY

A case of sudden death in a child suffering from paroxysmal ventricular tachycardia is reported.

By analogy with other reported cases it may be assumed that during the few seconds preceding death the ventricles may have been in a state of fibrillation.

Definite pathologic changes were found in the conduction system. These were probably the result rather than the cause of the tachycardia, and may have been due to the repeated periods of anoxemia during the seizures.

The late Dr. Jampolis gave permission to report this case. Dr. O. Saphir made the postmortem examination, and Dr. L. N. Katz interpreted the electrocardiogams.

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SHAKESPEARE AND PEDIATRICS

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The genius of William Shakespeare has depicted so many shades of human emotions and has dealt so vastly with almost every conceivable phase of human activity that it is not at all surprising that the man who knew human beings so perfectly should have known something of the medicine of his day. He apparently was an omnivorous reader, gifted with the capacity for absorbing and making use of all his available knowledge. An apt quotation can be found in Shakespeare's writings on almost any subject one cares to think about. His writings comprise a great philosophic and psychologic encyclopedia, ever inexhaustible and ever stimulating.

> . . . it gave me present hunger
> To feed again, though full.[1]

Shakespeare's medical knowledge was not inconsiderable. He knew of the controversy between Paracelsus and the Galenic school; he was aware of the medical fads and quackeries of his day and was acquainted with many of the medical superstitions of his time. Many writers have dealt with these phases of Shakespeare's medical knowledge. Both John Moyes and Sir St. Clair Thomson have enumerated nearly all of the medical references in Shakespeare's plays, and Augustine O'Downey, in a short monograph privately printed in Waterford about 1909, made an attempt to collect all the Shakespearian references to syphilis under the title, "William Shakespeare: Syphilographer." In Shakespeare's plays are numerous references, medical and otherwise, which should be of interest to the pediatrician because they indicate both a knowledge and a lack of knowledge of pediatrics and point out a number of interesting pediatric beliefs and practices of Shakespeare's time. For this reason I thought that it might be of some interest to pick out those quotations which would have any pediatric allusions.

It is interesting that while there are seven physicians in the thirty-six plays they have very little to say of medicine or of medical beliefs.

The Cambridge text has been used for all quotations.

From the Department of Pediatrics, McGill University, and the Children's Memorial Hospital.

Read at the Thirteenth Annual Meeting of the Canadian Society for the Study of Diseases of Children, East Aurora, N. Y., May 31, 1935.

1. Cymbeline, act ii, scene 4.

True it is that the English physician in Macbeth refers to the laying on of hands by the king for the cure of the "evil."

> . . . . at his touch,
> Such sanctity hath heaven given his hand,
> They presently amend.[2]

And the physician in "Cymbeline" prepares one of Shakespeare's very useful drugs the administration of which brings on a condition simulating death; nevertheless the physicians in Shakespeare are for the most part very minor characters who play little or no part in the development of the drama and have, with one notable exception, nothing to say about the science and art of medicine. Dr. Caius, the French physician in "The Merry Wives of Windsor," is, in Sir Hugh Evans' phrase, "a cowardly knave who has no knowledge of Hippocrates and Galen." The rôle of Dr. Caius is in no way medical; he is a caricature of a physician. Quite the opposite, however, is Cerimon, the nobleman in "Pericles," who finds his greatest contentment in the study and practice of medicine, although his noble birth does not require him to occupy himself with such pursuits. In Sir St. Clair Thomson's opinion, there is "no nobler panegyric of our profession" than this speech of Cerimon's in which he gives his reasons for studying and practicing medicine.

> I hold it ever,
> Virtue and cunning were endowments greater
> Than nobleness and riches; careless heirs
> May the two latter darken and expend,
> But immortality attends the former,
> Making a man a god. 'Tis known, I ever
> Have studied physic, through which secret art,
> By turning o'er authorities, I have,
> Together with my practice,[3] made familiar
> To me and to my aid the blest infusions
> That dwell in vegetives, in metals, stones;
> And I can speak of the disturbances
> That nature works, and of her cures; which doth give me
> A more content in course of true delight
> Than to be thirsty after tottering honour,
> Or tie my treasure up in silken bags,
> To please the fool and death.[4]

2. Macbeth, act iv, scene 3.

3. "To study the phenomena of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all." (Osler, William: Books and Men, in "Aequanimitas, with Other Addresses to Medical Students, Nurses, and Practitioners of Medicine," Philadelphia, P. Blakiston's Son & Co., 1904.)

4. Pericles, act iii, scene 2.

With the possible exception of the reference to the healing of scrofula by the laying on of hands, none of the medical characters in Shakespeare's plays makes any references which could have pediatric bearing. These, whenever they occur, are part of the speeches of lay characters. The infant and the schoolboy, for instance, are referred to in the well known "seven ages speech."

> At first the infant,
> Mewling and puking in the nurse's arms.[5]

Mewling means "meowing" like a kitten, and puking has not changed its meaning, so that the description is thus quite suitable for the irregularly nursed, overfed infant, whining a bit after feeding at the breast and regurgitating a mouthful of his excess feeding. Then comes

> . . . the whining school-boy, with his satchel
> And shining morning face, creeping like snail
> Unwillingly to school.

This is a description too perfect to require comment. In this same connection one cannot pass over the description of the

> Last scene of all
> That ends this strange eventful history,
> Is second childishness and mere oblivion,
> Sans teeth, sans eyes, sans taste, sans everything.

But to return to the infant, Shakespeare's plays abound in references to infants, infancy and nursing, and there is one particular reference to weaning with which I shall attempt presently to deal at some length. There is nothing exceptional in Shakespeare's mentioning the fact that a new-born infant cries with his first breath, but when this is made the means of King Lear expressing his bitterest cynicism in a sublime phrase it becomes worthy of note.

> Thou must be patient; we came crying hither:
> Thou know'st, the first time that we smell the air,
> We wawl and cry. I will preach to thee: mark.
> . . . . .
> When we are born, we cry that we are come
> To this great stage of fools.[6]

Here is a world of sorrow, a life of frustration and disillusionment. All the accumulated bitterness of disappointment is embodied in a single sentence based on the first cry of a new-born infant.

Cesarean section is twice referred to. In each instance it is posthumous section, the only type practiced in ancient days of which I have

5. As You Like It, act ii, scene 7.
6. King Lear, act iv, scene 6.

any knowledge. In "Cymbeline," Imogen's husband is called Posthumus, and the ghost of his dead mother cries:

> Lucina lent me not her aid,
> But took me in my throes;
> That from me was Posthumus ript,
> Came crying 'mongst his foes,
> A thing of pity![7]

Ript is probably an aptly descriptive term for such an operation. It connotes the haste with which the infant was obviously removed from the opened uterus of the dead or almost dead mother. Lucina, mentioned in the last quotation, is the Roman goddess of light, or the goddess who brings into the light, and hence the deity who watches over women in labor. She is referred to in "Pericles" as the

> Divinest patroness and midwife gentle
> To those that cry by night.[8]

In "Cymbeline" the fact of Posthumus' unnatural birth had no bearing on the development of the drama; in "Macbeth," however, the fact has the force of an ambiguous oracle. The three witches have told Macbeth that

> . . . none of woman born
> Shall harm Macbeth.[9]

So in the final act in the encounter with Macduff, Macbeth says:

> I bear a charmed life, which must not yield
> To one of woman born.[10]

Macduff has the disarming answer:

> Despair thy charm
> And let the angel whom thou still hast served
> Tell thee, Macduff was from his mother's womb
> Untimely ripp'd.

There are similar references to prematurity, such as "sent before my time" in "Richard III," but none of them contain anything more than a mere mention of the fact.

Sir John Falstaff uses his rotundity to refer to the rounded belly of the young infants:

> My lord, I was born about three of the clock in
> the afternoon, with a white head and something
> a round belly.[11]

7. Cymbeline, act v, scene 4.
8. Pericles, act iii, scene 1.
9. Macbeth, act iv, scene 1.
10. Macbeth, act v, scene 8.
11. 2 Henry IV, act i, scene 2.

In "The Winter's Tale" occurs a passage which is interesting for its pediatric errors. King Leontes unjustly denies the paternity of his new-born princess, Perdita. Paulina, the lady-in-wating to the queen, brings in the new-born babe to demonstrate to all how much the child resembles the father. Even the smiles and frowns of the hour old child are like the father's, says Paulina.

> Behold, my lords,
> Although the print be little, the whole matter
> And copy of the father, eye, nose, lip;
> The trick of's frown; his forehead; nay, the valley,
> The pretty dimples of his chin and cheek; his smiles;
> The very mould and frame of hand, nail, finger.[12]

This represents a somewhat free use of poetic license.

Many references occur to nursing at the breast of either the mother or the wetnurse. Lady Macbeth apparently nursed her own children:

> I have given suck, and know
> How tender 'tis to love the babe that milks me:
> I would, while it was smiling in my face,
> Have plucked my nipple from his boneless gums,
> And dash'd the brains out, had I so sworn as you
> Have done to this.[13]

Several passages, however, make reference to a long held belief that the character of the nurse can be passed on to the infant through the milk. The Duchess of York says of her son:

> He is my son; yea, and therein my shame;
> Yet from my dugs he drew not this deceit.[14]

Coriolanus' mother says the same to him:

> Thy valiantness was mine, thou suck'dst it from me,
> But owe thy pride thyself.[15]

From time immemorial, mothers have admitted that their children inherited only good qualities from them. "He doesn't get it from my side of the family" is an ancient defense which even Shakespeare knew how to express. Juliet's nurse expresses the same idea:

> . . . were not I thine own nurse
> I would say thou hadst suck'd wisdom from thy[16] teat.[17]

12. The Winter's Tale, act ii, scene 3.
13. Macbeth, act i, scene 7.
14. Richard III, act ii, scene 2.
15. Coriolanus, act iii, scene 3.
16. The folio reading is "thy teat," but other emendations suggested "my teat" and "another teat," either of which makes better reading.
17. Romeo and Juliet, act i, scene 3.

The closing scene of "Antony and Cleopatra" contains a reference to the nurse falling asleep with the infant at her breast. The asp has bitten Cleopatra in the breast, and she is dying:

> Peace, peace!
> Dost thou not see my baby at my breast
> That sucks the nurse asleep? [18]

The allusion is easily recognizable—the infant fed without regard to time, nursing so long that both nurse and infant fall asleep. Finally, the following may be taken as a reference to sudden death in a nursing infant:

> Here could I breathe my soul into the air,
> As mild and gentle as the cradle-babe,
> Dying with mother's dug between its lips.[19]

Coming now to weaning, there is in the garrulous speeches of Juliet's nurse an accurate account of an old established mode of weaning an infant from the breast. This method is by no means obsolete in many European countries; particularly is it still practiced in many of the Baltic states. When the child is between 2 and 3 years of age, on a given day and at a given time, the mother will offer the breast to her unsuspecting child. She will first have the nipple thoroughly sprinkled with pepper. The child takes the nipple, begins to suck and lets go with a savage scream, much to the delight of all the onlookers. In a few hours the peppered nipple is again offered and again accepted by the unwary child. This usually suffices. A very stupid child will accept the offered breast a third time. It would be interesting to know from Latvian, Lettish and Lithuanian psychiatrists what psychosexual maladjustments they attribute to this strange practice. Juliet, according to the story, was weaned in this manner when she lacked about a fortnight of 3 years of age:

> . . . but, as I said,
> On Lammas-eve at night shall she be fourteen;
> That shall she, marry; I remember it well.
> 'Tis since the earthquake now eleven years;
> And she was wean'd—I never shall forget it—
> Of all the days of the year, upon that day:
> For I had then laid wormwood to my dug,
> Sitting in the sun under the dove-house wall;
> My lord and you were then at Mantua:—
> Nay, I do bear a brain:—but, as I said,
> When it did taste the wormwood on the nipple
> Of my dug, and felt it bitter, pretty fool,
> To see it tetchy, and fall out with the dug! [20]

18. Antony and Cleopatra, act v, scene 2.
19. 2 Henry VI, act iii, scene 2.
20. Romeo and Juliet, act i, scene 3.

The nurse talks on till she is told to keep quiet, but she reveals many interesting details.

> Susan and she,—
> Were of an age: well, Susan is with God;

This indicates that she was engaged as a wetnurse because her own child died while she was still nursing. She also makes the following interesting statement:

> And since that time it is eleven years;
> For then she could stand high-lone;[21] nay, by the rood,
> She could have run and waddled all about;

The nurse remembers that it was eleven years since she weaned the 3 year old Juliet because "she could stand high-lone." Most infants in Shakespeare's day must have had rickets, and late standing, walking and dentition must have been so usual as to be regarded as normal. For instance, the young Duke of York makes the following observation:

> 'Twas full two years ere I could get a tooth.[22]

A common nursery scene, that of the child falling, hitting its head and raising a lump on its forehead, is described by the same nurse in "Romeo and Juliet."

> For even the day before, she broke her brow:
> . . . . . .
> And yet, I warrant, it had upon its brow
> A bump as big as a young cockerel's stone;
> A perilous knock; and it cried bitterly.[23]

A reference to child marriage occurs in the same scene, Juliet's mother saying:

> Well, think of marriage now; younger than you
> Here in Verona, ladies of esteem,
> Are made already mothers. By my count,
> I was your mother much upon these years
> That you are now a maid.

"Romeo and Juliet" is further interesting to the pediatrician because of a reference to a well known superstition with regard to the cutting of the matted hair over the infant's occiput. Queen Mab, who is the fairies' midwife and who comes

> In shape no bigger than an agate-stone
> On the fore-finger of an alderman.[24]

21. In later emendations, "alone" occurs.
22. Richard III, act ii, scene 4.
23. Romeo and Juliet, act i, scene 3.
24. Romeo and Juliet, act i, scene 4.

is a creature who does many queer things. She rides through lovers' brains, over the lawyer's fingers and controls their dreams. She is also

> . . . that very Mab
> That plats the manes of horses in the night,
> And bakes [25] the elf-locks in foul sluttish hairs,
> Which once untangled much misfortune bodes.

The idea that untangling matted hair can bring ill luck is still held to this day by many otherwise moderately intelligent people. With some it is bound up with the Samson myth denoting loss of strength if cut off, while with others the matted hairs seem to be bound up with good fortune. Taboos with regard to hair, not only children's hair, are too varied and too numerous to recount in a short paper, but it seems likely that the reference in the Queen Mab speech originates in an ancient Russian belief in a goblin that plats, not the "manes of horses in the night" but the manes of the grooms who sleep in the stables, and these plats too must not be untangled or cut off lest ill luck follow.

As to congenital malformations, many are referred to in Shakespeare's works. Particularly are they made use of to harmonize the deformed body with the deformed soul of Richard III, who is a veritable clinical repository of congenital defects.

> . . . since the heavens have shaped my body so
> Let hell make crook'd my mind to answer it.[26]

He speaks of his being prematurely born, with a withered arm, legs of an unequal size, hunchback and teeth. These deformities are referred to in a group of passages in "Henry VI" and "Richard III," all of which are very well worth complete quotation. In the following, the opening speech in "Richard III," he mentions only his being born prematurely and refers generally to his deformities without specifying any of them.

> But I, that am not shaped for sportive tricks,
> Nor made to court an amorous looking-glass;
> I, that am rudely stamp'd, and want love's majesty
> To strut before a wanton ambling nymph;
> I, that am curtail'd of this fair proportion,
> Cheated of feature by dissembling nature,
> Deform'd, unfinish'd, sent before my time
> Into this breathing world, scarce half made up,
> And that so lamely and unfashionable
> That dogs bark at me as I halt by them;

25. In later emendations, "makes" occurs.
26. 3 Henry VI, act v, scene 6.

It is, however, in "Henry VI" that he and Henry reveal most of Richard's physical deformities. Richard says:

> Why, love foreswore me in my mother's womb:
> And, for I should not deal in her soft laws,
> She did corrupt frail nature with some bribe,
> To shrink mine arm up like a wither'd shrub;
> To make an envious mountain on my back,
> Where sits deformity to mock my body;
> To shape my legs of an unequal size;
> To disproportion me in every part,
> Like to a chaos, or an unlick'd bear-whelp
> That carries no impression like the dam.[27]

Here there are mentioned the withered arm (Erb's palsy?), the legs of an unequal size (congenital dislocation of the hip?) and the envious mountain on the back (congenital absence of vertebral bodies?). Shakespeare, having no doubt seen isolated instances of these deformities, combined them in the wicked Richard to give psychologic justification for his evil spirit. In the following passage he describes his having been born by footling presentation and refers to his having been born with teeth:

> I, that have neither pity, love, nor fear.
> Indeed, 'tis true that Henry told me of;
> For I have often heard my mother say
> I came into the world with my legs forward:
> Had I not reason, think ye, to make haste,
> And seek their ruin that usurp'd our right?
> The midwife wonder'd, and the women cried
> "O, Jesus bless us, he is born with teeth!"
> And so I was; which plainly signified
> That I should snarl and bite and play the dog.[28]

That Richard III was born with teeth is mentioned again by Queen Margaret to the Duchess of York, Richard's mother.

> From forth the kennel of thy womb hath crept
> A hell-hound that doth hunt us all to death:
> That dog, that had his teeth before his eyes,
> To worry lamb and lap their gentle blood,
> That foul defacer of God's handiwork.[29]

And finally Henry VI's closing speech before his death at Richard's hand:

> The owl shriek'd at thy birth,—an evil sign;
> The night-crow cried, aboding luckless time;
> Dogs howl'd, and hideous tempest shook down trees;
> The raven rook'd her on the chimney's top,

27. 3 Henry VI, act iii, scene 2.
28. 3 Henry VI, act v, scene 6.
29. Richard III, act iv, scene 4.

> And chattering pies in dismal discords sung.
> Thy mother felt more than a mother's pain,
> And yet brought forth less than a mother's hope,
> To wit, an indigested and deformed lump,
> Not like the fruit of such a goodly tree.
> Teeth hadst thou in thy head when thou wast born,
> To signify thou camest to bite the world: [30]

The young Duke of York also refers to his uncle having been born with teeth:

> Marry, they say my uncle grew so fast
> That he could gnaw a crust at two hours old: [31]

In the beautiful song closing "A Midsummer Night's Dream," Puck prays that the happily united couples have offspring without physical defects:

> And the blots of Nature's hand
> Shall not in their issue stand;
> Never mole, hare lip, nor scar,
> Nor mark prodigious, such as are
> Despised in nativity,
> Shall upon their children be.[32]

The seemingly mad Edgar in "King Lear" attributes these and other misfortunes to the foul fiend Flibbertigibbet:

> This is the foul fiend Flibbertigibbet: he begins
> at curfew and walks till the first cock; he gives
> the web and the pin, squints the eye and makes
> the hare-lip; mildews the white wheat and hurts
> the poor creature of earth.[33]

The "web and the pin" refers to a disease of the eye, probably some form of cataract or corneal scar causing a web over the field of vision. There is another reference to this disease in "The Winter's Tale."

> . . . all eyes
> Blind with the pin and web.[34]

The word "pin" in this sense is somewhat obscure.

The whole tragedy of the falsely accused Imogen in "Cymbeline" hinges on the discovery of a mole, which could have been a supernumerary nipple, by her betrayer.

> . . . under her breast—
> Worthy the pressing—lies a mole, right proud
> Of that most delicate lodging: [35]

30. 3 Henry VI, act v, scene 6.
31. Richard III, act ii, scene 4.
32. A Midsummer Night's Dream, act v, scene 2.
33. King Lear, act iii, scene 4.
34. The Winter's Tale, act i, scene 2.
35. Cymbeline, act ii, scene 4.

No reference is made in the play to the side on which the mole is found, but in the source story, which is the ninth story of the second day of the "Decameron," the mole is placed on the left side, which agrees with the experience of most clinicians, namely, that rudimentary nipples are far more common on the left side.

Of the diseases interesting to the pediatrician Shakespeare has not a great deal to say. There are references, however, to the contagiousness of diseases, to the greater susceptibility of the young to infection, to "meazles," to epilepsy, to chlorosis and to rheumatism. The contagiousness of diseases is several times spoken of, humourously by Falstaff:

> It is certain, that either wise bearing, or ignorant carriage, is caught, as men take diseases, one of another: therefore, let men take heed of their company.[36]

and plaintively, as in "A Midsummer Night's Dream:"

> Sickness is catching: O, were favour so,
> Yours would I catch, fair Hermia, ere I go;[37]

But it is in "Hamlet" that there occurs this important observation:

> The canker galls the infants of the spring
> Too oft before their buttons be disclosed,
> And in the morn and liquid dew of youth
> Contagious blastments are most imminent.[38]

The only references susceptible of an interpretation as an allusion to any of the "contagious blastments" of young children as they are known today is one in "Coriolanus":

> How! no more?
> As for my country I have shed my blood,
> Not fearing outward force, so shall my lungs
> Coin words till they decay against those meazles,
> Which we disdain should *tetter* us, yet sought
> The very way to catch them.[39]

Whether measles refers to present-day measles or is used merely as a vague term indicating any one of the exanthemas cannot be definitely decided, but judging from the general confusion about all exanthemas almost to Sydenham's time, it is doubtful if Shakespeare could have known of any such distinctions: Measles, tetter and smallpox, apparently were all one.

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36. 2 Henry IV, act v, scene 1.
37. A Midsummer Night's Dream, act i, scene 1.
38. Hamlet, act i, scene 3.
39. Coriolanus, act iii, scene 1.

Shakespeare has two epileptic characters, Julius Caesar—" 'Tis very like; he hath the falling-sickness," [40] and Othello—

> My lord is fall'n into an epilepsy:
> This is his second fit; he had one yesterday.

Note Iago's excellent treatment:

> The lethargy must have his quiet course:
> If not, he foams at mouth, and by and by
> Breaks out to savage madness. Look, he stirs: [41]

The "green sickness," or chlorosis, is mentioned several times, usually as a disease of females, e. g., "Now, the pox upon her green-sickness for me!" [42] or "a kind of male green-sickness;" [43] also:

> And with a green and yellow melancholy,
> She sat like patience on a monument.[44]

In "Antony and Cleopatra," however, Shakespeare seems to forget that the green sickness is a disease of females, for

> Lepidus
> Since Pompey's feast, as Menas says, is troubled
> With the green sickness.[45]

Rheumatism was, of course, thought to be entirely a climatic disease.

> And youthful still! in your doublet and hose this raw rheumatic day! [46]
> To dare the vile contagion of the night,
> And tempt the rheumy and unpurged air
> To add unto his sickness? [47]

But the following sentence seems to be a reference to arthritis deformans: "Aches contract and starve your supple joints! [48] Of course the word rheumatism had no direct relationship to any disease affecting the joints but referred rather to the catarrh of the nose.

On child training there is nothing of significance in Shakespeare's plays, save one line in "Othello":

> Those that do teach young babes
> Do it with gentle means, and easy tasks.[49]

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40. Julius Caesar, act i, scene 2.
41. Othello, act iv, scene 1.
42. Pericles, act iv, scene 6.
43. 2 Henry IV, act iv, scene 3.
44. Twelfth Night, act ii, scene 4.
45. Antony and Cleopatra, act iii, scene 2.
46. The Merry Wives of Windsor, act iii, scene 1.
47. Julius Caesar, act ii, scene 1.
48. Timon of Athens, act i, scene 1.
49. Othello, act iv, scene 2.

Shakespeare had a great deal to say about syphilis, and some of his descriptions of syphilitic lesions are so exact as to suggest a very intimate knowledge of this disease, which in his day was sweeping Europe; but he did not seem to realize the effect of the syphilitic virus on the progeny; hence his plays do not enlighten one at all on congenital syphilis. Nevertheless, Shakespeare's excursions into syphilography would form a very interesting chapter in medical history.

I have attempted in my poor way to assemble from references and from my own readings a number of Shakesperian quotations having some interest to the pediatrician. They shed some light on interesting customs and beliefs as well as on the extent of pedriatic knowledge in Shakespeare's time. It is just another evidence of the great mind of the greatest poetic genius, the man whom Emerson called the Emperor of the Mind, whose genius

> . . . filled all measure
> Of heart and soul, of strength and pleasure.

Shakespeare has enriched every phase of thought and human action. His pediatric contributions illustrate but another facet of this many-sided colossal intellect.

News and Comment

GENERAL

Memorial to Dr. Ruhräh.—A memorial room was opened in the building of the Medical and Chirurgical Faculty of Maryland on January 21 in honor of the late Dr. John Ruhräh of Baltimore. The room was furnished by friends of Dr. Ruhräh, principally outside the medical profession, and it is hoped ultimately to make this room a replica of the one in which he lived and worked for the last twenty-five years of his life. Many of his own books have been placed in the room, which will be formally dedicated at the annual meeting of the faculty in April. The opening of the room was a feature of the meeting of the Osler Historical Society. Dr. Sanford V. Larkey, librarian of the Welch Medical Library of Johns Hopkins University, spoke on "Children and Witches," and Dr. John Rathbone Oliver presented "An Unpublished Autograph Letter of Dr. John Crawford." Dr. Ruhräh, who died March 10, 1935, provided in his will that most of his estate will eventually go to the faculty.

National Tuberculosis Association.—During the month of April the National Tuberculosis Association will put on an educational campaign to emphasize the following aspects of tuberculosis: (*a*) the discovery of tuberculosis in its early stages and the need for going to the physician promptly when symptoms are first apparent and (*b*) anticipating tuberculosis among youth of high school and college age by examination with the tuberculin test and the roentgen rays.

Clinical Course in Pediatrics, University of Vienna.—The advanced course by the medical faculty of the University of Vienna will be given as usual this year from May 4 to 16. Following this and extending from May 18 to 30 there will be a clinical course in pediatrics, taking in all phases. The honorarium for this course is 900 schillings (approximately $175).

PERSONAL

Dr. José Bonaba has been named professor of the children's medical clinic at Montevideo to replace the late Professor Morquio.

CORRECTIONS

In the abstract of the article by Dr. Engelbach and Dr. Schaefer, entitled; "Endocrine Dwarfism," which appeared in the January issue (Am. J. Dis. Child. **51**:171, 1936), the words "does not" in the fifth line from the bottom of the page should be omitted, making the sentence read, "These studies led to the conclusion that the extract employed contains a growth hormone, and that thyroid extract is a valuable adjunct in this form of treatment."

In the article by Dr. John A. Toomey, entitled "The Seventh Nerve as a Possible Pathway for the Transmission of the Virus of Poliomyelitis," which appeared in the January 1936 issue (**51**:58, 1936), the sentence beginning with line 9 on page 67 should read:

That there was a nuclear lesion of the sixth nerve was probable, since the external rectus muscle was paralyzed and there were jerking nystagmic movements of the opposite eye when the internal rectus muscle of this eye was contracted.

And the following statements should be added:

These symptoms usually signify the presence of a pontile lesion which has involved the association centers in the posterior longitudinal bundle or the fibers coming to the bundle from the nucleus of the sixth nerve. They are not present with the ordinary palsy of the sixth nerve seen in cases of meningitis in which only the peripheral portion of the nerve is involved and in which the association fibers and centers are intact.

Obituaries

WILLIAM PERRY NORTHRUP, M.D.
1851–1935

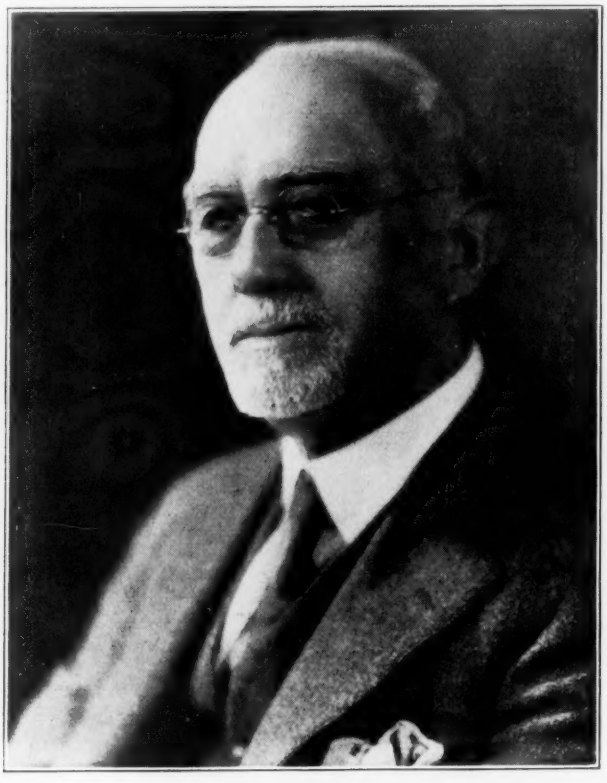
William Perry Northrup was born in Peterborough, N. Y., on Jan. 11, 1851, and died in New York on Nov. 20, 1935.

He received the degree of Bachelor of Arts from Hamilton College in 1872 and of Master of Arts in 1875. He attended Columbia University College of Physicians and Surgeons, receiving the degree of Doctor of Medicine in 1878. He was a member of the Alpha Delta Phi fraternity. From 1872 to 1876 he was instructor in Greek in Knox College, Galesburg, Ill., from which institution he received the degree of Doctor of Law in 1920.

After his graduation in medicine, Dr. Northrup served as an intern in the Roosevelt Hospital and soon began to work in the New York Foundling Hospital and the Presbyterian Hospital. In the New York Foundling Hospital he spent much of his time in the pathologic laboratory. In Abt's "Pediatrics" it is said that he performed the largest number of autopsies on infants of any man of his period. He was closely associated with O'Dwyer in perfecting intubation, a procedure which has saved numberless lives in cases of laryngeal diphtheria. Dr. Northrup wrote many papers for medical journals on diverse pediatric subjects—on infant feeding, infectious diseases (particularly diphtheria), scurvy, sclerema, tuberculosis and pneumonia. Among the diseases which interested him most and about which he loved to teach were pneumonia, empyema and scurvy. The emphasis placed by Dr. Northrup on lobar as the common type of pneumonia, even in infants, made a strong impression on many. The simple intercostal incision for empyema in infants was strongly advocated by him, as saving the infant from shock and from osteomyelitis of the rib when a resection is done. He stressed fresh air treatment in cases of pneumonia and developed the plan of keeping delirious patients outdoors on balconies or on roofs. He edited the American edition of Ashby and Wright's textbook, "The Diseases of Children, Medical and Surgical," and contributed articles to Nothnagel's "Encyclopedia of Practical Medicine." There are over fifty reprints catalogued under his name in the library of the New York Academy of Medicine. His writing was always vivid and informal, and it was by these qualities that he made his points forceful.

Dr. Northrup was a founder and the president of the American Pediatric Society, a member emeritus of the American College of Physicians, president of the Pediatric Section of the New York Academy of Medicine and a member and the president of the New York Pathological Society.

He was adjunct professor of pediatrics in the Bellevue Hospital Medical College from 1893 to 1896, professor of pediatrics in New



WILLIAM PERRY NORTHRUP
1851—1935

York University, University and Bellevue Hospital Medical College until 1920, and emeritus professor of this institution until his death. He was consulting physician to the Willard Parker Hospital, the New York Foundling Hospital, the Infant Asylum, the Seaside Hospital, the Washington Heights Hospital, the Babies Hospital, Newark, N. J., the New York State Reconstruction Home, West Haverstraw, N. Y., and the Vassar Brothers Hospital, Poughkeepsie, N. Y.

After his retirement from teaching he continued to practice but gradually gave up active work and lived quietly with his nieces. He was married twice, both wives dying before his death.

Dr. Northrup was attending physician to the Presbyterian Hospital for over twenty-five years. He served his regular turn in the wards for adults during much of this period, but the adults never touched his heart; he spent much more time with the few patients in the small ward for children than with the adults in his service. Nevertheless, he knew a great deal about some of the diseases of adults from his long experience in the hospital, and he frequently surprised the members of the house staff by making a diagnosis which had been entirely missed by other members of the visiting staff. He never pretended to knowledge that he did not have. He did know many things well, and his information was manifest in many surprising ways.

No formal record of his life can give posterity a picture of this man. He was tall, spare and extremely vigorous, even up to the last few years of his long life, and he always gave the impression of boundless energy, of unquenchable youth.

Dr. Northrup was an enthusiast, and his teaching was never dull, except to those who underrated him because of his exuberance, because of his tricks of pedagogy and because he was frankly not interested in many things. He had a lovable disposition and a keen sense of humor. He was always cheerful and was most considerate of those who worked with him. His influence will long be felt among his students and his associates.

C. H. S.

WILLIAM BRADBURY McCLURE, M.D.

1884—1936

Through the untimely death of Dr. McClure, pediatricians have lost an earnest fellow practitioner, and medicine a scientist of unusual ability. His place cannot be easily filled, and to many who knew him best the loss seems irreparable.

William Bradbury McClure was born on Aug. 7, 1884, at McKeesport, Pa. He died at Evanston, Ill., on Feb. 13, 1936, at the age of 51.

He received the degree of Bachelor of Science at the Gettysburg College in 1908 and the degree of Doctor of Medicine at the Johns Hopkins University four years later. Following this he served his internship in pediatrics at the Johns Hopkins Hospital for one year. The next two years were spent at the Children's Memorial Hospital in Chicago, as resident physician. During the following year he filled the position of instructor in pediatrics at the University of Iowa.

After this preliminary training, Dr. McClure moved to Evanston, where he became associated with Dr. Henry F. Helmholz and Dr. Louis W. Sauer in the practice of pediatrics. This relationship was broken, however, by Dr. McClure's service in the United States Army. From the time of his return until his death he continued the practice of pediatrics in Evanston.

He took an active part in the work of the Infant Welfare Society, caring for one of its stations during most of his life. He was on the staff of the Evanston Hospital, where he was attending pediatrician until his death. In addition, he was associate attending physician at the Children's Memorial Hospital, where he spent a great deal of his time. For several years he was director of the activities of the Otho S. A. Sprague Memorial Institute at the Children's Memorial Hospital. To round out his general service to humanity, he also devoted much of his time to the teaching of undergraduate students at the Northwestern University Medical School, where he was associate professor in pediatrics, to the teaching of postgraduate students at the Children's Memorial Hospital and to the teaching of nurses at the Evanston Hospital.

Dr. McClure was a valued member of the American Medical Association, the American Pediatric Society, the American Academy of Pediatrics, the Chicago Pediatric Society, the Central States Pediatric Society and the Institute of Medicine of Chicago, and through this branch, of the Chicago Medical Society.

Dr. McClure's investigative work led him into varied fields. In his early days he wrote about such subjects as the effect of clothing

on heat stasis and the chemistry of the urine, particularly the citric acid content. He was always interested in the physiology of the skin, and in his work on the intradermal salt solution test he investigated the loss as well as the absorption of water through the skin. His mind turned from the investigation of the toxicity of tri-nitrotoluene to such surgical problems as the technic of intestinal anastomosis. Probably his best known interest was that of the mechanism of edema, on which subject he wrote several papers of lasting value. Only those who knew him best realize the great number of projects which his death will leave unfinished. He was always interested in research on several subjects at the same time, and some of the problems occupied his mind for many years.

Dr. McClure developed in his personality an almost unique combination of traits. He possessed an inquiring type of mind and was always searching for new ideas and unearthing false concepts in established beliefs. At the same time, this progressive urge was balanced by a severely conservative censorship. This resulted in the meticulous care which characterized all of his work, investigative and clinical, and made his judgment invaluable. He was practically always on the correct side of any diagnostic controversy. In his relationship to his fellows, he exhibited much the same attitude of mind. While he himself was rigidly honest and straightforward, his judgment of others was delightfully tolerant.

During the past few years he worked under a cloud of ill health, which made him seem to lack his old force. He was aware of his arterial disease and, sensibly, tried to protect himself. His scientific usefulness really terminated in the summer of 1935, when he suffered a serious cerebral attack, which left him dazed and vague for several months. A rare personality was blotted out at that time.

C. A. A.

Abstracts from Current Literature

Anatomy and Physiology

THE PRENATAL INCIDENCE, STRUCTURE AND DEVELOPMENT OF SOME HUMAN SYNOVIAL BURSAE. B. MARDEN BLACK, Anat. Rec. **60**:333, 1934.

Subcutaneous bursae do not develop before birth. The subfascial and subtendinous prepatellar bursae are not present till after birth. The subacromial bursa is present after the third month of fetal life.

SNELLING, Toronto, Canada.

A HISTOLOGIC STUDY OF THE ANATOMIC STRUCTURES FORMING THE ORAL CAVITY. WILLIAM H. G. LOGAN, J. Am. Dent. A. **22**:3 (Jan.) 1935.

The surgical anatomy of the jaws, particularly from the standpoint of operations for cleft palate, is discussed from the observations in stained microscopic sections of material obtained from twenty-seven specimens from persons ranging in age from birth to 15 years. The anatomic findings with respect to the attachments and direction of fibers of the muscles of the upper lip are of particular interest in connection with operations for harelip, as is also the arrangement of the germs of the deciduous and permanent teeth with respect to surgical procedures for cleft palate.

NOYES, Chicago.

THE APPEARANCE OF BASOPHILIC GRANULES IN ERYTHROCYTES IN HEALTHY INFANTS IN MUKDEN. T. KUWANO and H. KONDO, J. Orient. Med. **22**:23 (Feb.) 1935.

The authors investigated the presence of basophilic granules in the erythrocytes of healthy Japanese and Manchu infants and drew the following conclusions from their microscopic observations:

1. Basophilic granules of the red cells were found in fifty-five (41.35 per cent) of one hundred and thirty-three healthy Japanese infants examined, and the highest percentage was 3.6.

2. Fifty-seven (71.25 per cent) of eighty healthy Manchu infants examined proved to have the granules. Although the highest percentage was 7, no sign could be found of lead meningitis or any similar disease as a cause of the increase of basophilic erythrocytes.

3. The percentage in either Japanese or Manchu boys was always a little higher than that in girls.

4. In both Japanese and Manchu infants the highest percentage was found at the age of from 5 to 10 months, and the rate seems to fall gradually with increasing age.

5. The quantity of lead taken by an infant has a great deal to do with the cause of lead meningitis. However, the authors conclude that the climate in Manchuria seems to play an important part in holding the disease back.

LESLIE, Evanston, Ill.

Pathology, Bacteriology and Biochemistry

THE PLACE OF BACTERIAL ALLERGY IN THE IMMUNIZATION PROCESS. L. DIENES, J. Bact. **29**:28 (Jan.) 1935.

After making observations on the sensitization of normal and tuberculous guinea-pigs, Dienes states that it is important to keep in mind that allergy produces mainly a cellular reaction in the tissues which come in contact with the antigen,

consisting mostly of mononuclear cells. In those diseases in which allergy persists, as in tuberculosis, the defensive reaction is mainly a tissue reaction. Once antibodies are formed, the reaction in the tissues to the antigen is a quick exudation. The influence of allergy on the tissue reaction is probably present also in acute diseases. But the allergy probably serves a more general purpose. The inefficacy of serum therapy in most diseases makes it probable that the active immunization of the tissues, and not the diffusion of antibodies, is the most powerful factor in the healing, and the bacterial allergy is a manifestation of the early phase of the process of active immunization.

STOESSER, Minneapolis.

ENDOGENOUS INFECTIONS BY CLOSTRIDIUM WELCHII. LUCILLE C. LYNCH and PAUL F. CLARK, J. Bact. **29**:36 (Jan.) 1935.

The possibility of an endogenous origin for gas gangrene infections led the authors to make a thorough study, the results of which may be presented in the following outline form:

1. Distribution of Clostridium Welchii in the animal body.

(*a*) Clostridium Welchii was isolated from twelve of fourteen human livers obtained at autopsy; eight of the specimens were removed within six hours post mortem. In only one case was a pathologic condition of the liver present.

(*b*) Clostridium Welchii was isolated from eight of fifteen livers removed during life from dogs during operative procedure.

(*c*) Clostridium Welchii was isolated from the meconium of ten infants during the second day of life.

2. Experimental endogenous infections with Clostridium Welchii.

(*a*) Clostridium Welchii was isolated in cases of peritonitis produced in laboratory animals by the intraperitoneal injection of sterile bile.

STOESSER, Minneapolis.

THE INCIDENCE AND SIGNIFICANCE OF MINUTE HEMOLYTIC STREPTOCOCCI. PERRIN H. LONG and ELEANOR A. BLISS, J. Bact. **29**:39 (Jan.) 1935.

Long and Bliss isolated from the throats of 80 per cent of persons ill with glomerular nephritis and 50 per cent of persons ill with rheumatic infection minute beta hemolytic streptococci. These organisms are rarely found in the throats of persons ill with chronic disease or acute infections. Their incidence in normal human beings is from one half to one third of the incidence of ordinary beta hemolytic streptococci. In both glomerular nephritis and rheumatic infection more cultures from the throat were positive for minute hemolytic streptococci than for ordinary beta hemolytic streptococci. In many persons suffering from these diseases, only minute hemolytic streptococci were recovered from cultures from the throat during the period of investigation. In view of the well known association of these two diseases with infection with the beta hemolytic streptococcus it is believed that these findings assume an added importance.

STOESSER, Minneapolis.

CYTOLOGIC STUDIES ON RHEUMATIC FEVER: II. CELLS OF RHEUMATIC EXUDATES. CURRIER MCEWEN, J. Clin. Investigation **14**:190 (March) 1935.

The amount, character and cellular content of exudates from patients with rheumatic fever were studied in relation to various aspects of the disease and were compared with those of nonrheumatic exudates. No specific character could be assigned to exudates in rheumatic fever.

GUEST, Cincinnati.

AGGLUTININS FOR SHEEP AND RABBIT ERYTHROCYTES IN HUMAN SERA. C. A. STUART, J. TALLMAN and E. G. E. ANDERSON, J. Immunol. **28**:75 (Feb.) 1935.

Seven hundred and sixty normal human serums were studied for sheep and rabbit erythrocyte agglutinins. A relationship was shown between the titers of

these two agglutinins. It was also shown that there is a difference in titer, depending on the temperature of the agglutinin. The titer for both agglutinins is definitely higher at 5 C. than at 37 C. Furthermore, there was a significant sexual difference in human serums with respect to these two agglutinins. The serums of females contained a higher agglutinin content than those of males.

FOTHERGILL, Boston.

SHEEP AND RABBIT CELL AGGLUTININS IN HORSE SERUM SICKNESS AND INFECTIOUS MONONUCLEOSIS. C. A. STUART, J. TALLMAN and E. BRINTZENHOFF, J. Immunol. **28**:85 (Feb.) 1935.

It was shown that during horse serum sickness in man there is an increase in the titer of both rabbit and sheep erythrocyte agglutinins. The sheep cell agglutinins can be removed by successive absorptions with some nonspecific antigen such as rabbit cells. There is essentially no increase in rabbit cell agglutinins in the serums of persons with infectious mononucleosis. The authors conclude that the increase in sheep cell agglutinins during horse serum sickness is not due to Forssman antibodies.

FOTHERGILL, Boston.

Nutrition

FOLLICULAR LESIONS IN VITAMIN A AND C DEFICIENCIES. MAX SCHEER and HARRY KEIL, Arch. Dermat. & Syph. **30**:177 (Aug.) 1934.

The authors report two cases of scurvy with follicular lesions and point out that in the early stages the follicular lesions in cases of vitamin A deficiency clinically resemble those in cases of vitamin C deficiency. Regarding the pathologic characteristics of the two lesions the following summary is made: "In vitamin A deficiency, the chief effect is in the epithelium of the epidermis and of the hair follicles. Vascular pathologic change is insignificant, and hemorrhage does not seem to occur. In scurvy, however, the vascular factor is the most prominent feature, and it is this which serves to produce the distinguishing characters." Both lesions respond quickly when the diet is adequate.

DULIN, Iowa City.

METABOLIC DISTURBANCES IN RELATION TO THE TEETH. CHARLES F. BODECKER, Bull. New York Acad. Med. **10**:553 (Sept.) 1934.

Until recently, the only preventive treatment instituted to protect the dental mechanism against destruction has been an attempt to promote cleanliness of the oral cavity. If such cleanliness of the oral cavity is defined as sterility, an attempt to attain it can be regarded as futile. Many false notions exist among medical and dental practitioners regarding the structure and function of the dental tissue and its individual parts, and it is only in the past few years that account is being taken of the nutritional phases in their relation to the formation and preservation of teeth.

Experimental reports show that dental caries can be controlled by dietary means. This is true especially among children, although there is much divergence of opinion regarding specific beneficial factors in the diet. Acid-forming foods (carbohydrates) are generally indicted as predisposing to a high incidence of caries.

Contributory factors in dental decay are: (*a*) systemic disorders, such as rickets, diabetes and acidosis; (*b*) dietary deficiencies, such as lack of mineral salts, vitamins, proteins and lipins; (*c*) hereditary influences, and (*d*) endocrine disturbances. One or more of the these conditions result in insufficient protection of the teeth against decay of the pulp. Predisposing and exciting factors are (*a*) anatomic defects of the teeth, (*b*) abnormal saliva and (*c*) unsanitary conditions of the mouth (bacteria and the retention of food).

JAHR, Omaha.

INFANT NUTRITION: SOME PRINCIPLES FOR INFANTS AND ADULTS. JESSE R. GERSTLEY, Illinois M. J. **66**:280 (Sept.) 1934.

After a ten years' study of the reaction and flora of the feces for different types of infant feeding, Gerstley concludes that the essential factor is the creation of an intestinal condition favorable to the growth of the Acidophilus flora and unfavorable to flora of the putrefactive type. This, he believes, can be accomplished only by adding lactose in the quantity in which enough acid will be furnished by its fermentation to overcome the alkalinizing properties of the diet. The addition of acid to cow's milk may make the combination easier for gastric digestion; it has no effect on the amount of acid in the stool or on the intestinal flora.

BARBOUR, Peoria, Ill.

FUNDAMENTALS OF INFANT FEEDING. CLIFFORD G. GRULEE, Illinois M. J. **66**:288 (Sept.) 1934.

For the vast majority of infants breast feeding is to be preferred. The period just after birth is often the time during which it is determined whether the child shall be kept on the breast. Breast feeding should be as carefully supervised as artificial feeding. When it is necessary to put a child on the bottle a simple formula is satisfactory in the vast majority of instances. There is no objection to the use of special preparations, provided the man who prescribes them knows how to use them. In Dr. Grulee's opinion there is, however, definite objection to the claim that these preparations are better than any others simply because of the results of experiments of one kind or another, for the usefulness of such preparations is not to be judged by experimentation on animals or by the results in the test tube. Finally, as in every other situation which confronts the physician, the final test is his judgment in the given case.

BARBOUR, Peoria, Ill.

THE ACIDOSIS OF GUANIDINE INTOXICATION. A. S. MINOT, KATHARINE DODD and J. M. SAUNDERS, J. Clin. Investigation **13**:917 (Nov.) 1934.

These studies on the effects of guanidine intoxication in dogs constitute an important corollary to the studies on the rôle of guanidine intoxication in infants with alimentary intoxication, reported earlier by Minot and Dodd in the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

Guanidine hydrochloride was administered subcutaneously to dogs kept on a low calcium diet. The intoxication thus induced was characterized by: (1) muscular tremors and convulsions, apparently due to the decreased physiologic effectiveness of calcium ions in the presence of guanidine in the body; (2) vomiting and diarrhea, and (3) a marked fall in the p_H and alkali reserve of the blood, associated with an increased amount of lactic acid in the blood and in the urine. It was argued that the acidosis was due primarily to increased production and defective metabolism of lactic acid. The administration of alkalinizing salts in the treatment of the acidosis was attended with unusual difficulties because of the danger associated with a temporary decrease in the effectiveness of calcium ions in the presence of increased guanidine. It was shown that the administration sodium lactate (in doses calculated on the basis of the formula of Hartmann and Senn) failed to increase the alkali reserve of the blood because of the inability of the subject to utilize lactates and that from 10 to 20 per cent of the dose of sodium lactate administered intravenously was excreted in the urine. Sodium bicarbonate, while at times both dangerous and ineffective if used alone, could be made safe and promptly efficient if calcium medication (such as the use of calcium gluconate) was combined with its administration. Gradual relief of acidosis resulted from calcium medication alone or combined with the parenteral administration of fluids such as a solution of dextrose or physiologic solution of sodium chloride. The most satisfactory treatment for the acidosis (and that recommended also for the control

of acidosis in clinical subjects with hyperguanidinemia) was the use of sodium bicarbonate combined with repeated intravenous calcium medication and the liberal use of fluids to increase the output of urine.

GUEST, Cincinnati.

INGESTION OF STAPHYLOCOCCUS EXOTOXIN BY HUMAN VOLUNTEERS, WITH SPECIAL REFERENCE TO STAPHYLOCOCCIC FOOD POISONING. C. E. DOLMAN, J. Infect. Dis. **55**:172 (Sept.-Oct.) 1934.

The experience of the author would indicate that food poisoning from Staphylococcus is relatively rare and is probably produced by only a few strains. The metabolite produced by the staphylococcus that is responsible for the poisoning is not an exotoxin.

TOOMEY, Cleveland.

PARENTERAL USE OF CAROTENE IN THE TREATMENT OF VITAMIN A DEFICIENCY IN ALBINO RATS. FU-TANG CHU and HARRIET COADY, J. Pediat. **5**:75 (July) 1934.

Carotene injected intramuscularly was effective in curing rats of vitamin A deficiency. However, the effect of carotene injected intramuscularly was somewhat slower than the action of carotene given by mouth. When chronic diarrhea was produced in rats with vitamin A deficiency the injection of carotene by the intramuscular route was of decided help in supplementing the oral administration. It is suggested that the use of carotene by parenteral injection be employed in cases of vitamin A deficiency associated with faulty fat metabolism, such as that in chronic diarrhea, obstruction of the bile ducts, pancreatic dysfunction, etc.

LEMASTER, Evanston, Ill.

CHRONIC HYPOGLYCEMIA IN CHILDHOOD. BENJAMIN KRAMER, H. G. GRAYZEL and CHARLES I. SOLOMON, J. Pediat. **5**:299 (Sept.) 1934.

Two cases of chronic hypoglycemia in small children are reported. The first child had enlargement of the liver with extensive fatty infiltration, but no glycogen was present in the liver. Other hepatic functions except glycogenesis were apparently normal. It is suggested that in this case dextrose was converted into fat because of inability to form glycogen. The second child presented organic changes in the nervous system as well as hypoglycemia. It was uncertain whether the damage to the nervous system caused hyperinsulinism or whether pancreatic hyperinsulinism caused the changes in the nervous system. Both children were studied intensively, and full laboratory data are included.

LEMASTER, Evanston, Ill.

THE CLINICAL STATUS OF VITAMIN D MILKS. JOHN W. M. BUNKER and ROBERT S. HARRIS, New England J. Med. **211**:1140 (Dec. 20) 1934.

The authors discuss and appraise the available evidence concerning the value of vitamin D milks in respect to their antirachitic effect when fed to infants. It is their opinion that both yeast milk and irradiated milk, as they are today obtainable on the market, have been proved to be valuable in the cure and prevention of rickets when used in the amounts and in the manner usually indicated for milk in infant feeding, that the more carefully controlled experiments fail to show any distinct difference in the relative efficacies of the two types of milk expressed in terms of their potencies in rat unit equivalents and that, in view of this fact, it is reasonable to expect more antirachitic benefit from the type of milk which offers the larger number of units per quart.

Before Zucker milk can be evaluated in terms comparable with those for the two other kinds of vitamin D milk under discussion, more clinical data must be available.

GENGENBACH, Denver.

A Five-Year Clinical Study of the Prophylactic Value of Antirachitic Agents. Adolph G. De Sanctis and John Dorsey Craig, New York State J. Med. **34**:712 (Aug. 15) 1934.

Both cod liver oil in liquid form and cod liver oil concentrate in the form of tablets gave better results than viosterol. The writers believe that rickets is not due to deficiency of vitamin D alone but that vitamin A is also an important factor in the disease.

Aikman, Rochester, N. Y.

Further Studies on Growth and the Economic Depression. Carroll E. Palmer, Pub. Health Rep. **49**:1453 (Dec. 7) 1934.

This paper is the third dealing with variations of the increase in weight for elementary school children in Hagerstown, Md. In the first paper it was shown that the averages for actual weight did not vary significantly from year to year during the period from 1921 through 1927. In the second paper it was shown that the actual weights for children in the same city were not, after several years of severe economic depression, materially decreased in 1933. In this study for 1934, the averages for weight show no striking difference from those for previous periods. The variability of weight for boys is about the same as in the earlier periods, but for girls the weight is more variable in both 1933 and 1934. Also there is a slight increase in the proportion of girls (12 per cent) below the average weight. Average normal gains for the years 1933 and 1934 are lower than similar gains calculated for the period from 1921 to 1927.

Leslie, Evanston, Ill.

Hypervitaminosis D Rickets. A. W. Ham and L. D. Murray, Brit. J. Exper. Path. **15**:228, 1934.

Young rats receiving very large daily doses of vitamin D showed rachitic lesions in the long bones after three weeks. As the matrix which formed in the bones during the experiment was poorly calcified, it was concluded that the administration of large amounts of vitamin D inhibited the normal process of calcification in the bones. As osteoclasts were not prominent in the histologic picture, the poor calcification could not be attributed to them. The phenomena observed can be explained best, it is thought, by the theory that vitamin D in some way increases the attraction of the blood for calcium. The results are compatible with, although they do not directly support, the theory that vitamin D acts through the intermediary of the parathyroid mechanism to control a fraction of the serum calcium.

From the Authors' Summary.

Recurrent Vomiting Attacks in Childhood. K. H. Tallerman, Brit. M. J. **2**:767 (Oct. 27) 1934.

A brief general discussion is given the condition, the signs and symptoms, the precipitating causes, the history of the patient and the family in respect to allergy and the results of the cutaneous tests, blood counts and tests of gastric acidity. Special emphasis is placed on the association of headache with the attacks of vomiting, and the belief is expressed that the attacks are atypical manifestations of migraine.

Royster, University, Va.

Obesity in Childhood. R. W. Ellis and K. H. Tallerman, Lancet **2**:615 (Sept. 15) 1934.

Fifty children between the ages of 5 and 14 years whose weight was found to be not less than 25 per cent above the average for both the age and height form the basis of this study. Twenty-five were girls and twenty-five were boys. The onset of obesity in the largest group was between the ages of 7 and 10 years. All the children showed a tendency to overeat, particularly carbohydrate foods. In three cases the condition dated from scarlet fever and in one from mumps. A familial incidence of obesity was recorded in thirty instances.

The patients were examined with particular reference to the distribution of the obesity, the presence of striae atrophicae, the genital development, the secondary sexual characters, the condition of the fundi and visual fields and the blood pressure. A stereoscopic roentgenogram was taken of the sella turcica; urinalysis was made, and in thirty-eight instances a dextrose tolerance test was carried out.

The arbitrary classification into endocrine, endogenous and exogenous types is thought to have a certain value if the limitations of the classification are recognized and the terms defined.

If it is admitted that excessive obesity cannot occur in the absence of an adequate intake of calories and fluid in relation to the output of energy and that, therefore, an exogenous factor operates to some extent in every case, there remains, nevertheless, a considerable group of cases in which the occurrence of obesity at a particular age period or a marked family history of the condition suggests that a primary endogenous factor may be at work as well.

No endocrine therapy was used in these cases as no evidence of statural or genital infantilism was found. A tendency to girdle distribution of fat was seen in cases of both endogenous and exogenous origin. In the majority of cases considerable elevation of the systolic blood pressure was shown.

Dietetic treatment should be undertaken only in cases in which the obesity gives rise to symptoms, and it should never be sufficiently rigid to interfere with normal growth.

Treatment with thyroid or pituitary extracts is held to be contraindicated in the absence of definite evidence of hypothyroidism or statural and genital infantilism, respectively.

LANGMANN, New York.

GEE'S DISEASE. T. I. BENNETT, Lancet **2**:739 (Oct. 6) 1934.

The author prefers the name Gee's disease to that of celiac disease as the second term is usually applied only to the form occurring in children. Two instances are cited in girls aged 17 and 21 years, respectively. Both patients gave a history of steatorrhea and tetany during childhood, and one showed rather pronounced deformities of the bones and a tendency to the development of dangerous anemia.

A diet low in fats, the administration of calcium and proper treatment of the accompanying anemia are recommended.

LANGMANN, New York.

CRANIOTABES IN FOUR-MONTHS-OLD TWINS. K. H. TALLERMAN, Proc. Roy. Soc. Med. **27**:1324 (Aug.) 1934.

Craniotabes was found to be present in twins of 4 months. Roentgenograms of the wrists of both children showed active rickets. The Wassermann reaction in each case was negative.

WILLIAMSON, New Orleans.

THE SURGICAL IMPORTANCE OF KETOSIS AND CYCLIC VOMITING. G. F. FISMER, South African M. J. **8**:524 (July 28) 1934.

Fismer points out the danger of operation in the presence of ketonemia. In discussion of the subject he adopts Frew's classification of the four stages of carbohydrate starvation as responsible for ketonemia: 1. Gross carbohydrate starvation. The complete omission of carbohydrate is associated with the administration of anesthetics and persistent vomiting (congenital pyloric stenosis, intracranial disease, acute intestinal obstruction and other acute abdominal conditions and certain diseases of the urinary system). 2. Failure of digestion of the carbohydrates in an ordinary diet, which occurs in cases of emotional upset and change in the character of the food consequent to admission to the hospital and during travel. 3. Failure of absorption of carbohydrates in a limited group of cases of no surgical interest. 4. Failure of carbohydrate metabolism, such as occurs in cases of postanesthetic poisoning and cyclic vomiting.

The clinical picture of cyclic vomiting is described, and the differential diagnosis of this condition and acute intestinal obstruction (especially the type due to

volvulus when the obstruction is high), acute appendicitis, recurrent enteric intussusception and uremia is discussed.

GONCE, Madison, Wis.

THE BIBLIOGRAPHIC BALANCE SHEET OF THE REGIMEN OF RAW FRUITS IN THE TREATMENT OF DIARRHEAS IN INFANTS AND CHILDREN. M. SCHACTER, J. de méd. de Paris **54**:766 (Sept. 6) 1934.

The use of a diet consisting exclusively of raw fruit with the possible addition of sweetened tea was described first in 1929 by Heisler and by Moro. The author lists innumerable articles on the use of this regimen. In all the articles except that by D. Corda (*Lattante* **4**:436, 1933) excellent results are reported.

LESLIE, Evanston, Ill.

VOMITING IN EARLY INFANCY. M. M. L. RIBADEAU-DUMAS and BARNAUD, Nourrisson **22**:226 (July) 1934.

Four cases of severe and persistent vomiting are described in infants ranging in age from 1 month to 6 years. The roentgen examinations showed partial obstruction of the third portion of the duodenum. The duodenal site of obstruction was also demonstrable by the presence of bile in the vomitus.

In all these cases the patient was greatly helped or cured by being placed in the ventral position after meals. The explanation in these cases is that in the dorsal position there is constriction of the duodenum by the superior mesenteric artery, which is relieved or alleviated by the simple expedient of a change of position after eating.

MCCLELLAND, Cleveland.

PHYSIOPATHOLOGIC CHANGES AND TREATMENT IN CASES OF THE DIARRHEAS OF INFANCY. J. CATHOLD and A. BOSQUET, Paris méd. **2**:360 (Nov. 3) 1934.

The authors discuss the changes in the motor and secretory activities of the gastro-intestinal tract in cases of diarrhea due to various causes. The dyspepsias are considered from the point of view of the physiopathologic changes brought about by parenteral infection and dietary errors and of the probable reactions to varying types of feeding in the presence of an altered physiologic state. The article concludes with a discussion of irritative diarrheas and diarrheas due to underfeeding.

LESLIE, Evanston, Ill.

RACHITISM AND LYMPHATISM. N. ULRICH-LÉVY, Progrès méd., no. 45, Nov. 10, 1934, p. 1745.

This article presents nothing new. The value of vitamins and proper hygiene in both conditions is emphasized. In some cases of lymphatism endocrine therapy is suggested.

LESLIE, Evanston, Ill.

A HISTOPHYSIOLOGIC STUDY OF INFANTILE RICKETS. A. POLICARD, M. PÉHU and J. BOUCOMONT, Rev. franç. de pédiat. **10**:722, 1934.

This careful study of the histologic changes in rickets under the direction of Péhu reveals the following facts:

In rickets the normal evolution of the epiphyseal cartilage in undergoing degeneration and death is lacking. The cartilaginous cells persist, and the interstitial substance shows increased affinity for water but lacks affinity for calcium salts. Consequently, there is invasion of this tissue by numerous capillaries, and the ossification which takes place resembles that noted in connective tissue or callus formation.

From a physiologic standpoint calcification reveals two distinct phases. In the first, under the action of a special ferment phosphatase, the calcium phosphoric esters brought by the blood are decomposed, and the inorganic calcium salts are liberated in the interstitial spaces. In the second phase, a special preosseous,

protein-like substance absorbs the calcium salts and becomes true bone. In cases of rickets, the phosphatase was found to be present in greater quantities than normal; what is lacking seems to be a sufficient supply of calcium phosphoric esters. It is possible, however, that the utilization of these esters is at fault and that a toxic product inhibits the action of the phosphatase. Understanding of the rachitic process is far from complete.

The article comprises forty pages; it is well presented and beautifully illustrated.

LESLIE, Evanston, Ill.

Prenatal Conditions

CONGENITAL PARTIAL HEMIHYPERTROPHY: REPORT OF CASE INVOLVING THE RIGHT LOWER EXTREMITY ONLY. LOUIS J. BRAGMAN, Arch. Pediat. **52**:53 (Jan.) 1935.

A congenital type of hemihypertrophy is reported which is nonhandicapping and apparently nonprogressive. The presumptive ease with which this case, because of the mildness of the hypertrophy, could be overlooked implies that similar cases probably are not being recognized.

AUTHOR'S SUMMARY. (WADDELL JR., University, Va.)

CONGENITAL ABSENCE OF PENIS. ROBERT B. DRURY and HENRY H. SCHWARZELL, Arch. Surg. **30**:236 (Feb.) 1935.

A case of congenital absence of the penis is described in a 13 year old white boy. The boy had no symptoms. The urine was voided through the rectum. Except for this abnormality the boy was normal. Urography disclosed the presence of bilateral hydro-ureter.

KAISER, Rochester, N. Y.

DIAPHRAGMATIC HERNIA AT THE ESOPHAGEAL HIATUS, SHORT ESOPHAGUS AND THORACIC STOMACH. P. E. TRUESDALE, New England J. Med. **212**:240 (Feb. 7) 1935.

After reporting and discussing in detail a number of cases, Trueslale offers a new theory as to the origin of congenital short esophagus and thoracic stomach, namely, that enlarged esophageal hiatus or any other congenital aperture in the diaphragm occurs as a result of embryologic failure of fusion. Almost invariably, thoracic stomach is the result of herniation through a congenital hiatus hernia and may occur at any time after birth. The short esophagus is the result of cessation of traction on it by the stomach, which has assumed a position in the thorax, and in many instances a short esophagus of a few centimeters is the result of inflammatory changes at its lower end.

GENGENBACH, Denver.

CONGENITAL FUSION OF ASTRAGALUS AND SCAPHOID: BILATERAL; INHERITED. ABRAHAM S. ROTHBERG, JOEL W. FELDMAN and OTTO F. SCHUSTER, New York State J. Med. **35**:29 (Jan. 1) 1935.

A case of this rare orthopedic condition is reported in a girl 8 years of age.

AIKMAN, Rochester, N. Y.

COARCTATION OF THE AORTA: ITS IMPORTANCE AND DIAGNOSIS. W. KENDRICK PURKS and W. PIERRE ROBERT, South. M. J. **28**:158 (Feb.) 1935.

Coarctation of the aorta is not very rare. Clinically, the major diagnostic feature is a discrepancy between the degree of pulsation and the level of blood pressure readings in the upper extremities and those of the lower extremities, the former showing much larger values. Roentgenographic examination of the chest gives positive diagnostic evidence in the majority of cases.

SCHLUTZ, Chicago.

DYSCHONDROPLASIA (OLLIER'S DISEASE), WITH REPORT OF A CASE. DONALD HUNTER and PHILIP WILES, Brit. J. Surg. **22**:507 (Jan.) 1935.

There is an increasing tendency at the present time to regard all congenital lesions of the growing ends of bone as being manifestations of the same primary defect. In this article the authors state that on careful examination of roentgenograms it is possible to distinguish a number of points of difference, especially from diaphyseal aclasis, which is a hereditary condition. In Ollier's disease there is little evidence of this.

They understand Ollier's achondroplasia to be a disease of the growing ends of bones in which the normal ossification of cartilage fails to take place, so that as the bone increases in length there remain in the diaphyses areas of cartilage which do not ossify. The process is not primarily one of tumor formation, although in some cases, particularly in the long bones of the hands and feet, there may be hyperplasia of cartilage. The disease shows a tendency to be unilateral.

The etiology of Ollier's achondroplasia is unknown.

The long bones, such as the humerus, radius, ulna, femur, tibia and fibula, are those in which the typical appearances of this condition are to be seen. The more rapidly growing end of the bone shows the most marked changes. The center of the shaft usually appears normal. A good description of the roentgenologic appearances of the bone is given. It concerns chiefly translucent areas in the bone. At times the diaphysis is broadened, and small exostoses may appear near the end of the diaphysis. The affected bones show shortening and some bowing. As the child grows older the typical striped translucent appearance disappears and is replaced by a speckling due to islands of dense calcification.

There are no changes in the blood calcium or phosphorus. The actual age at onset is not known, but some abnormality is often first noticed between the first and second years of life when, as a rule, one limb is found shorter than its fellow. By about 6 years of age bending of the limbs or enlargement of one or more fingers is apparent. In the early stages the epiphyses are not involved but may become so after the fifth year, so that in time a uniform picture is presented. Calcification begins after the sixth year. The prognosis is good except for the deformities present. A case is cited in which the condition was present in a child 7 years of age.

SUMMERFELDT, Toronto, Canada.

DOUBLE PLACENTA PRAEVIA AND PRE-NATAL DIAGNOSIS OF CONGENITAL HEART IN SUCCESSIVE LABOURS. E. K. MACLELLAN, Brit. M. J. **1**:14 (Jan. 5) 1935.

A woman aged 41, a nonipara, was admitted to the hospital for profuse bleeding. Placenta praevia was diagnosed and cesarean section performed. Binovular twins were found, with double placenta praevia. The twins were well developed and survived. The mother made a satisfactory convalescence.

Three years later the same patient was readmitted to the hospital. She was in labor. She had not reported to the clinic for antepartum examination, but the history was essentially negative. Before delivery auscultation of the fetal heart showed a prolonged pause in the pulse beat after 4 or 8 regular beats. The baby was delivered with low forceps and had a peculiar purplish color, not due to cyanosis. A postnatal diagnosis of partial heart block was confirmed. The patient died, however, about six months later, and at autopsy there was an irregular-shaped patent foramen ovale; there was no pulmonary stenosis, but attached to the pulmonary artery were the remains of the stenosed and obliterated ductus arteriosus. It was presumed that the bundle of His was interfered with by the congenital anomaly, the proximity being close.

ROYSTER, University, Va.

CONGENITAL OESOPHAGEAL STRICTURE. W. M. FELDMAN, Proc. Roy. Soc. Med. **28**:410 (Feb.) 1935.

A case of this condition in a boy, 1½ years of age, is reported.

WILLIAMSON, New Orleans.

CONGENITAL LESION OF HEART ON PERICARDIUM. H. V. MORLOCK, Proc. Roy. Soc. Med. **28**:759 (April) 1935.

A patient aged 2 years and 9 months was found on examination to have impaired percussion in the first and second interspaces immediately to the right of the sternum. The apex beat was in the fourth interspace in the midclavicular line. A roentgenogram showed a large opaque mass with a well defined rounded margin, extending from the mediastinum into the field of the right lung under the screen. The upper part pulsated but appeared to be distinct from the lower part of the shadow, which also pulsated. On thoracoscopic examination both the anterior and the posterior mediastinum were seen to be clear of any form of tumor or glands. This examination left no doubt that the cause of the shadow was within the pericardium, and in view of the child's age and the absence of previous illness it seemed fair to assume that the lesion was of congenital origin.

WILLIAMSON, New Orleans.

FETAL EXTRASYSTOLES OBSERVED IN UTERO. BARRE and HENRIET, Bull. Soc. d'obst. et de gynéc. **24**:74 (Jan.) 1935.

Numerous extrasystoles, occurring so frequently as to give the fetal heart tones marked irregularity, were observed on auscultation during the eighth month. Delivery occurred somewhat prematurely in the middle of the ninth month. There was marked hydramnio. The infant weighed 2,300 Gm. and was delivered by forceps because of uterine inertia. The infant cried at birth, and on auscultation only one extrasystole was heard every 10 beats. At the age of 10 hours only an occasional extrasystole could be heard on prolonged auscultation. Over a further period of eighteen days no cardiac irregularity except sinus arrhythmia could be observed. At the age of 4 months the infant was observed to have developed normally. There was no evidence of congenital syphilis. The authors believe that the cardiac irregularity observed in utero was reflex in origin, perhaps due to compression of the fetus by the hydramnio.

GLASER, Rochester, N. Y.

Diseases of the New-Born

PRECOCIOUS DENTITION IN THE NEWLYBORN; REPORT OF A CASE. LEE COHN and JOHN MOTT RECTOR, Arch. Pediat. **52**:121 (Feb.) 1935.

The case of a healthy infant born with two lower central incisor teeth is reported, and an embryologic résumé of the development of teeth is given.

WADDELL JR., University, Va.

INFECTIONS IN THE NEW-BORN. W. H. CHASE, Canad. M. A. J. **32**:2 (Jan.) 1935.

In postmortem examinations of 445 new-born infants during the past five years there was gross or microscopic evidence of infection in 119 cases. In 132 cases there was evidence of intracranial trauma. Eighty-one per cent of the infections were pneumonias.

The various types of pneumonia, such as those due to metastatic infections, aspiration infections and bronchial and peribronchial infections without a known focus, are discussed.

MOORE, Omaha.

GANGRENE OF AN EXTREMITY IN A NEWBORN INFANT. F. CURTIS DOHAN, J. Pediat. **5**:756 (Dec.) 1934.

A case of gangrene of the left foot and lower part of the leg in an infant 13 days old is reported. No definite cause for the condition could be found. In reviewing the literature on this subject twenty-five similar instances were found.

Trauma, infected or noninfected embolism, constricting amniotic bands and angiospasm seemed to play a causative part in some of the cases.

LeMaster, Evanston, Ill.

Auricular Flutter in a Newborn Infant. Jules Sherman and Robert A. Schless, J. Pediat. **5**:802 (Dec.) 1934.

A case of auricular flutter diagnosed in an infant 1 month of age is reported. Sherman and Schless believe that the condition was present at birth, because during pregnancy the fetal heart tones were very rapid, and when the infant was 2 days old the roentgen rays showed cardiac enlargement. At 1 month of age dyspnea, cyanosis of the nails and a cardiac apex rate of 256 were found. The electrocardiogram demonstrated auricular flutter. The auricular rate was 464 beats per minute, and the ventricular rate was 232. At the age of 3 months the auricular rate was 420 and the ventricular rate was 210. Tincture of digitalis was given. The heart rate gradually dropped to normal.

LeMaster, Evanston, Ill.

Post Mortem Cesarean Section. Wilbur E. Hoffman, West Virginia M. J. **31**:78 (Feb.) 1935.

A single white woman, aged 25, was admitted to the hospital at 4:15 p. m., because of dyspnea and edema. She was first seen at 8:30 p. m. in labor and expired at 11:40 p. m. in convulsion. There was no response to resuscitative treatment. Postmortem cesarean section was done at 11:51, and a girl weighing 7 pounds 14½ ounces (3,387.7 Gm.) was delivered in about from fifteen to thirty seconds. The baby responded to artificial resuscitation within one minute and left the hospital in two days in good condition.

Shawkey, Charleston, W. Va.

Asphyxia Neonatorum: Its Treatment by Tracheal Intubation. J. B. Blaikley and G. F. Gibberd, Lancet **1**:736 (March 30) 1935.

Although the ordinary methods of treating asphyxia by clearing the upper respiratory passages and by providing an atmosphere of oxygen and carbon dioxide are entirely satisfactory in the majority of cases, it has seemed to the authors that occasionally a life is lost through failure of this ideal atmosphere to reach the lungs.

Their method consists in the use of a specially designed pharyngoscope (a modification of Howarth's Chevalier Jackson instrument) and the introduction of Magill's silk web endotracheal catheter not more than an inch (2.54 cm.) into the trachea. As the pressure obtained in the bronchial system depends not only on the pressure with which gas is delivered through the catheter but also on the ease with which it can escape through that part of the glottis not occupied by the catheter, the size of the latter is of importance. For premature infants of 5 pounds (2,267.96 Gm.) a no. 3 catheter is used, and for larger infants a no. 4. The rest of the apparatus consists of a device for delivering a mixture of carbon dioxide and oxygen.

This method is recommended only in cases in which respiratory movements do not quickly become established or in which, because of some mechanical obstruction in the larynx, trachea or bronchi, air is not drawn into the lungs.

Langmann, New York.

Adrenal Hemorrhage in the Normally Delivered Infant of a Diabetic Mother. Voron, Pigeaud and Cuche, Bull. Soc. d'obst. et de gynéc. **23**:536 (Oct.) 1934.

The mother had been previously pregnant six times; there were three miscarriages, and three infants died in the course of labor. Diabetes was diagnosed during the fifth pregnancy. During the last two pregnancies glycosuria disappeared from two to three months after delivery. The infant was normally delivered but

seemed in a mild state of shock, with slight cyanosis and slightly accelerated respirations. Cyanotic attacks recurred every three to four hours, and the infant died on the third day. At necropsy the most striking finding was the replacement of the right adrenal gland by a hemorrhagic mass the size of an orange, and a slight subarachnoid hemorrhage. The authors imply an association between the adrenal hemorrhage and the diabetes of the mother. The abstractor would like to know whether the glycosuria present only during and shortly after the last two pregnancies was true diabetes or lactosuria. GLASER, Rochester, N. Y.

EPIDEMIC PEMPHIGUS OR RITTER'S DISEASE OF THE NEW-BORN. DAVEO and BASSARGETTE, Bull. Soc. d'obst. et de gynéc. **24**:150 (Feb.) 1935.

The authors report an epidemic of bullous exfoliative dermatitis of the new-born. All degrees of the disease were observed and in all cases the condition developed in a similar manner. Erythematous patches of more or less intense redness appeared, followed immediately by the development of bullae. The contents of the bullae were clear at first but became cloudy. Direct smears showed only pus cells. Staphylococci were recovered only by culture. The bullae then peeled, giving the appearance of second degree burns, or, in extreme cases, that of a macerated living fetus. The details in six cases are given. Two infants died one week after the onset of the disease, with hyperthermia and in collapse, giving the impression of death due to an acute intoxication similar to that which occurs in burns. The authors state that they believe Ritter's disease to be only a peracute form of epidemic pemphigus of the new-born. GLASER, Rochester, N. Y.

ICTERUS OF THE NEW-BORN. PAUL GIRAUD, J. de méd. de Paris **55**:185 (Feb. 28) 1935.

Giraud discusses icterus of the new-born under the following headings: (1) benign or physiologic; (2) due to obstruction of the biliary passages; (3) due to infection. The article is well organized, but nothing new is presented.

LESLIE, Evanston, Ill.

HEINE-MEDIN DISEASE IN THE NEW-BORN. FERNANDO CISLAGHI, Pediatria **42**:1456 (Dec.) 1934.

A case of Heine-Medin disease in a new-born girl with the onset on the fifteenth day of life is reported because of the rarity of this condition. The clinical, physical, electrical and laboratory examinations clearly pointed out that the condition was in the paralytic period and that there was involvement of all the groups of muscles of the upper and lower extremities.

The author gives in detail the differential diagnosis between obstetric (traumatic) paralysis, congenital myotonia of Oppenheim, pseudoparalysis of Parrot and Heine-Medin disease. SIGNORELLI, New Orleans.

PURULENT COMPLICATIONS IN ERYSIPELAS OF THE NEW-BORN. N. CARRARA, Pediatria (**43**:184 (Feb.) 1935.

A case of erysipelas in a 12 day old new-born infant is reported in which complicating purulent arthritis of the knee was associated with a favorable influence on the erysipelas. SIGNORELLI, New Orleans.

Acute Infections

THE RECENT WAVE OF STREPTOCOCCAL INFECTION. H. L. WALLACE and A. BROWNLIE SMITH, Lancet **2**:1391 (Dec. 22) 1934.

This investigation confirmed the general impression regarding the increased incidence of acute rheumatic infection and acute mastoiditis during 1933 and 1934

in the district of Edinburgh. This was of particular interest in view of the exceptionally large epidemic of scarlet fever which occurred during this time. It must be emphasized, however, that the cases of rheumatism and mastoiditis referred to had no apparent connection with those of scarlet fever. All the cases of arthritis and mastoiditis arising as a direct complication of this disease were automatically included among the cases of scarlet fever. However, it is conceivable that some of the cases included under those of rheumatism or mastoiditis may have been in reality cases of missed scarlet fever. It would seem that during the period under discussion (January 1929-March 1934) some factors acted either to increase the virulence of Streptococcus haemolyticus or to lower the individual resistance to the organism.

LANGMANN, New York.

SCHICK TESTS IN NIGERIAN NATIVES. J. CAUCHI and E. C. SMITH, Lancet **2**:1393 (Dec. 22) 1934.

From 15 to 30 per cent of 1,454 native children in Lagos under the age of 10 years showed positive Schick reactions, while only 2 per cent of 298 over 10 years of age yielded positive reactions. Though clinical diphtheria is almost unknown, natural immunization by subclinical infection appears to be active.

LANGMANN, New York.

IMMUNISATION AGAINST DIPHTHERIA BY MEANS OF A SINGLE DOSE OF ALUM-PRECIPITATED TOXOID. E. A. UNDERWOOD, Lancet **1**:137 (Jan. 19) 1935.

One hundred and fifty-two persons with positive Schick reactions and negative Moloney reactions were given 1 cc. of alum-precipitated toxoid and had a final Schick test four weeks after the injection. One hundred and twenty-seven showed negative reactions after one month.

LANGMANN, New York.

PERTUSSIS VACCINE. H. BULL, M. J. Australia **2**:223 (Aug. 18) 1934.

Pertussis vaccine in doses of 1,000,000,000, 2,000,000,000, 4,000,000,000 and 8,000,000,000 bacilli given prophylactically at four day intervals at about the period of exposure to infection did not prevent whooping cough among young infants but appeared to affect favorably the course of the disease. In a group of older children, when it was administered at about the onset of the disease it appeared in some cases to modify the course.

GONCE, Madison, Wis.

THE RAW APPLE DIET IN THE TREATMENT OF DYSENTERY. P. A. EARNSHAW, M. J. Australia **2**:305 (Sept. 8) 1934.

Earnshaw gives a résumé of methods of using raw apple diets in the treatment of dysentery. Good results have always been obtained by this author's treatment when directions were accurately followed. Patients with ulcerative colitis, as well as those with dysentery, have been found to respond to this therapy. The author recommends giving a child twenty grated apples per day for from one to two days, with gradual transition to a normal diet. An apple powder may be substituted for apple pulp, using 1 teaspoonful to 4 ounces (113.39 cc.) of water. The action is similar to that of raw apple pulp, and it is more easily administered. It can be given with milk in mild cases. The manner of action of apple pulp is still uncertain.

GONCE, Madison, Wis.

SOME ASPECTS OF AN INFLUENZA EPIDEMIC (1933). K. W. STARR, M. J. Australia **2**:483 (Oct. 13) 1934.

Fifty-five cases of influenza pneumonia, in which the average age of the patients was 22 years, are considered. The onset was gradual, showing an atypical influenzal syndrome. Pneumonia was heralded by apathy, delirium, chills, vomiting, pyrexia,

leukocytosis and muddy pallor. The elevation in temperature was remittent, without remission of the increase in the pulse rate. The blood pressure was low, rising with improvement. The pulmonary signs were variable.

Abdominal pain, constipation, hiccough, pleural pain, urinary retention and herpes labialis were of frequent occurrence. The complications listed were otitis media, sinusitis, spreading pneumonia, parotitis, empyema, dendritic ulcer, meningitis and meningismus.

In the fatal cases (five) death occurred shortly after the onset. All these patients showed a picture of profound vasomotor collapse, with marked pallor, sweating, dyspnea, cyanosis, pyrexia and falling diastolic pressure. The cause of death was considered to be vasomotor rather than cardiac failure. At postmortem examination disorganization of the adrenal glands was always observed. Epinephrine was frequently used in an effort to combat vasomotor collapse.

GONCE, Madison, Wis.

PROPHYLAXIS OF MALARIA IN CHILDREN. E. CACACE, Bull. Assoc. internat. de pédiat. prevent. **4**:15 (Sept.) 1934.

At the fourth conference of this, the newest pediatric society, held in Lyons, France, the first topic for discussion was the prevention of malaria in the young. This discussion was opened by Prof. Ernesto Cacace, of the University of Naples. In a voluminous report he drew the attention of pediatricians to the pioneer work of the Italian school in the methods of teaching and practice of antimalaria hygiene, begun in 1906 and continued since that time at such important stations as Naples and Capua.

The program of the station's activity comprises: (1) instruction in antimalaria work, given by visiting professors from the center, and, in general, under the auspices of the minister of education, to teachers in the elementary schools, to students attending normal courses in agriculture, mining and other technical subjects and especially in elementary teaching, and (2) treatment of malaria-stricken pupils and treatment by quinine of teachers and pupils in areas where the disease is prevalent.

The reporter recalls the many national and international congresses at which he spoke of his ideas and of the work of the station, and especially the resolutions voted by the Third International Congress for School Hygiene at Paris in 1910, the Third American Child Congress and the First Brazilian Child Welfare Congress at Rio Janeiro in 1922.

He summarizes similar work carried out by other institutions in Italy and other countries, particularly in Algeria, India, Greece, the Argentine Republic and British Guiana. With regard to Italy, particular attention is called to the important educative and prophylactic work being done in the rural schools of the Roman Campagna, under the management of the Municipality of Rome and the Rural Schools Commission; to the antimalaria propaganda pursued in the peasant schools of the Pontine Campagna, in the schools of many communes of the region of Latium and in Balilla schools in the Basilicata, Calabria and Sicily, and to the excellent work, sent on foot by G. Rossi, of the indigenous Antimalaria Children's Colony of Maccarese.

As an example of what other countries are doing, he cites, in the first place, the prophylactic work established in Algeria under the competent direction of Edmond and Etienne Sergent.

While the author points out that the antimalaria hygiene has produced results that prove its usefulness, he insists that the work is not being pursued in all the countries in which the disease is present. He calls for the integral application and popularization of antimalaria hygiene in the schools and especially among the pupils of the institutions for children of preschool age and the elementary schools of regions where the disease is prevalent.

Having emphasized the fundamental principles of antimalaria propaganda in the school, he concludes that, with a view to promote school hygiene in all districts

where the disease is prevalent, particularly in elementary schools and institutions for children of preschool age, it appears necessary to assure: (1) a system of health education, notably the education of master and pupil, by a concrete method capable of forming habits, that is to say, by the exercise of hygienic routine; (2) the treatment and medicinal prophylaxis of master and pupil by a rigorous and rational method; (3) healthful conditions in the school and the home, with special attention to the use of mechanical means of protection; (4) scrupulous cleanliness of the food and clothing of the pupil; (5) mental fitness of the pupil; (6) the employment of all other means necessary to complete antimalaria prophylaxis.

AMESSE, Denver.

GENERALIZED ERYSIPELAS IN TWO MONTH OLD INFANT; MULTIPLE RESIDUAL ABSCESSES; PHARYNGOLARYNGEAL ABSCESS OF THE PYRIFORM SINUS OPENED SURGICALLY BY THE CERVICAL ROUTE; RECOVERY. ROUÈCHE, OMBRÉDANNE and CHAUSSÉ, J. de méd. de Paris **54**:785 (Sept. 13) 1934.

The content of this article is well indicated by the title.

LESLIE, Evanston, Ill.

RELAPSES AND RECURRENCES IN INFECTIOUS DISEASES. M. SCHACHTER, J. de méd. de Paris **55**:13 (Jan. 3) 1935.

Statistics vary considerably. Lichtenstein, in a study of 31,882 cases of scarlet fever, found relapses occurring in 1.1 per cent. Recurrence after a considerable interval varies according to different studies, between 1.1 per cent and 5.9 per cent. Measles recurs less frequently than scarlet fever, diphtheria more frequently.

LESLIE, Evanston, Ill.

PRIMARY MENINGITIS IN PAROTITIS IN A PATIENT WITH TUBERCLE BACILLI IN THE SPUTUM. T. MIRONESCO and P. FLORESCO, J. de méd. de Paris **55**:50 (Jan. 17) 1935.

The patient had severe headache, fever, a positive Kernig's sign and stiffness of the neck. The spinal fluid showed 112 lymphocytes and 2 polymorphonuclears per cubic millimeter. A presumptive diagnosis of tuberculous meningitis was made, because of the pulmonary findings of tuberculosis. No organisms were present in the spinal fluid, and three days later bilateral parotitis was diagnosed. The signs of meningeal irritation disappeared rapidly and did not return. The patient had cared for a child with mumps three weeks previously.

LESLIE, Evanston, Ill.

RHEUMATISM AND SCARLET FEVER. WAREMBOURG and CORNILLE, J. de méd. de Paris **55**:51 (Jan. 17) 1935.

Rheumatism in association with scarlet fever shows itself in three forms. The first, early in the course of a scarlet fever, requires only treatment to make the patient more comfortable, as there are almost never any sequelae. The second, the *forme tardive*, may have an associated endocarditis and should be treated with rest and large doses of salicylates. The third, which usually involves only one joint, is due to the presence of the organism in the lesion; it offers a bad immediate prognosis and requires surgical intervention.

LESLIE, Evanston, Ill.

MALARIA IN THE INFANT. V. GILLOT and C. SARROUY, Paris méd. **25**:33 (Jan. 12) 1935.

This communication comes from Algeria and deals principally with the infection of the fetus in utero with the malaria parasite. The authors believe that this

accounts for a large proportion of the cases of malaria in children in their district and that it is possible for the parasite to pass the normal placental barrier. They cite experimental work in sheep which harbor a similar parasite and show that the parasite may be present in large numbers in the fetal blood with no demonstrable placental injury.

LESLIE, Evanston, Ill.

THE EARLY DIAGNOSIS OF MEASLES: THE SIGN OF "THE EYE OF GLASS" AND THE SIGN OF "THE SEMILUNAR FOLD" OF E. MEYER. M. SCHACHTER, Rev. franç. de pédiat. **10**:616, 1934.

In certain children during an epidemic of measles Schachter has noted associated with a slight bronchitis and low febrile reaction an appearance of the eyes as though they were made of glass. This lasted from one to three days and was followed by a typical though very light case of measles. He also noted the increased turgescence of the semilunar fold described by E. Meyer, but this came later than the glassy appearance of the eyes.

LESLIE, Evanston, Ill.

ANTIDIPHTHERITIC IMMUNIZATION WITH TOXOID AND INJECTIONS OF ANTITOXIN. CARLO RAVASINI, Pediatria **42**: 1052 (Sept.) 1934.

With a view of collaborating on the work of Pontano in reference to the relative immunizing value of simultaneous injections of toxoid and antidiphtheritic serum, Ravasini conducted certain experiments which consisted of injection into a series of guinea-pigs and a careful analysis of the results obtained. He was able to arrive at the conclusion that the injection of toxoid followed in twenty-four hours by the injection of antidiphtheritic serum represents one of the best immunizing methods.

SIGNORELLI, New Orleans.

MEASLES COMPLICATING TYPHOID FEVER. LUIGI CARTAGENOVA, Pediatria **42**:1221 (Oct.) 1934.

Three cases of typhoid fever are reported, in each of which measles developed as a complication.

The author observes that the complicating disease produced certain modifications in the agglutination and points out the fact that the coexistence of these diseases makes the prognosis more unfavorable.

SIGNORELLI, New Orleans.

RARE PSYCHIC AND NEUROLOGIC SEQUELS IN TWO CASES OF ENCEPHALITIS FOLLOWING MEASLES. ROSARIO RUGGERI, Pediatria **42**:1329 (Nov.) 1934.

Two cases of encephalitis following measles are reported. In one case the clinical picture was very similar to that in epidemic encephalitis, while the second patient presented seizures (fits), high grade phrenasthenia and signs of adiposogenital dystrophy.

SIGNORELLI, New Orleans.

COMBINED ACTIVE AND PASSIVE IMMUNIZATION AGAINST DIPHTHERIA AND TETANUS. PIO RITOSSA, Pediatria **42**:1411 (Dec.) 1934.

The author presents an exhaustive résumé of the literature concerning the theories and knowledge of active and passive immunity and gives a detailed explanation of the experimental work of various authors in the field of immunization. Particular stress is given to the efforts of workers from von Behring's time to the present to establish protective immunity against diphtheria and tetanus. To the work of Pontano, Mari, Dopter and Sacquépée, the Clavels, Maloney, Ramon, Zoeller, Migliori and Ravasini the author adds his own experience and concludes by stating that it is not only practical but also safe and reliable to provide immunization against diphtheria and tetanus by simultaneous inoculations.

The clinical technic recommended by the author is as follows:

1. Simultaneous injections (but at different sites) of (*a*) the usual prophylactic dose of antitetanic serum and (*b*) the first dose (usually 1 cc.) of toxoid.

2. The injection of the second dose of toxoid from fourteen to sixteen days after the first.

3. The injection of the third dose of toxoid three weeks after the second.

The author checked the efficacious action of this method by demonstrating negative Schick reactions in all his cases.

SIGNORELLI, New Orleans.

CUTANEOUS REACTION TO DIPHTHERITIC TOXIN AND THE ANTITOXIN CONTENT OF THE BLOOD (LATE CONTRIBUTIONS TO THE STUDY OF THE ORIGIN OF DIPHTHERITIC ANTITOXIN). D. D'ANTONA and M. VALENSIN, Pediatria **43**:40 (Jan.) 1935.

The authors experimented with rabbits passively and actively immunized. They have observed that in the former, notwithstanding a greater quantity of antitoxin contained in the blood serum, the cutaneous reactions to diphtheria toxins are more frequently positive than in the latter.

They state, first, that the positive or negative responses to immunization are dependent not on the quantity of antitoxin in the blood serum but on organic reactivity; second, that diphtheria antitoxin is derived for the body tissues under specific stimulation, and, third, that active immunity is far superior to passive immunity.

SIGNORELLI, New Orleans.

TREATMENT OF POLIOMYELITIS WITH INJECTIONS OF ANTIRABIC VIRUS. J. BARLA-SZABÓ, Pediatria **43**:48 (Jan.) 1935.

This paper presents the theoretical principles indicating the treatment of poliomyelitis with antirabic vaccine, with a detailed discussion. The author describes his experience with seventeen patients whom he treated in the subacute stages and reports very encouraging though not conclusive results. In his series the cases of longest duration were those in which the paralysis was in the fifth and sixth weeks.

SIGNORELLI, New Orleans.

SOME CASES OF BOTH SCARLET FEVER AND A DISEASE OF THE TYPHOID-PARATYPHOID GROUP. F. CIANTINI, Riv. di clin. pediat. **32**:1367 (Nov.) 1934.

Ciantini reports two cases of typhoid fever occurring in the course of scarlet fever and one case of scarlet fever and paratyphoid fever occurring together. In the latter case the patient died.

HIGGINS, Boston.

CLASSIFICATION OF BRONCHOPNEUMONIA IN CHILDREN WITH PARTICULAR REFERENCE TO BRONCHOPNEUMONIA IN MEASLES. G. SANPAOLESI, Riv. di clin. pediat. **32**:1409 (Dec.) 1934.

During an epidemic of measles in 1932 the author observed thirty-four cases of bronchopneumonia. He divides them according to their clinical and pathologic characteristics into three groups.

GROUP I (Compensated Type).—Fifteen cases are reported; one child died. This type is characterized as follows: Few symptoms involve the body as a whole; involvement is usually of one lobe only; the general condition remains good; the heart is not appreciably affected; the pulse is strong and not very rapid; the respiration is increased in frequency and depth; the liver is not enlarged; little or no cyanosis is present, and the temperature follows an even course and falls when resolution of the pneumonia occurs.

GROUP II (Uncompensated Type).—Eleven cases are reported; six patients died. This type is characterized by symptoms affecting the patient as a whole, by

superficial breathing, weak and rapid pulse, cyanosis alternating with pallor and general asthenia of all the muscles. The chest shows râles over the entire pulmonary fields, and the temperature varies, chills and sweats occurring alternately. As the disease progresses small foci and later massive areas of consolidation appear; the heart tends to enlarge to the right; the heart sounds become weaker; the liver is enlarged; the abdomen becomes distended and ballooned with gas; the pallor increases, and the nervous system becomes involved, as is seen by restlessness and perhaps convulsions. The symptoms progress, pointing to a poor prognosis and often leading to death.

GROUP III (Toxic type).—Five cases are reported; four patients died. This type is characterized by general debility, marked cyanosis, superficial and perhaps periodic breathing, continuous fever and a rapid pulse rate. The thoracic findings are few in contrast to the serious general condition of the patient. Only a few râles are heard over the chest. Observations at necropsy show disseminated foci of bronchopneumonia and marked parenchymatous degeneration.

HIGGINS, Boston.

PROPHYLAXIS OF MEASLES. OCTAVIO DA VEIGA, Arch. de pediat., Rio de Janeiro **7**:1 (Oct.) 1934.

Da Veiga has had good success with maternal blood in the prophylaxis of measles, when convalescent serum was not available.

SANFORD, Chicago.

PATHOGENESIS AND PROPHYLAXIS OF BRONCHOPNEUMONIA IN DIPHTHERIA. CARLO COMBA, Boll. d. Ist. sieroterap. milanese **13**:769 (Oct.) 1934.

According to the clinical and experimental data, the author thinks that diphtheritic bronchopneumonia is due in the majority of cases principally to the action of the diplococci of Fränkel favored by a diphtheritic toxinfection. As a prophylaxis for this complication, he administers specific serum therapy to all patients with diphtheria as soon as possible. On the other hand, to curtail the action of the diplococcus, on a basis of numerous results obtained in the pediatric clinic of Florence, he devised a serum prophylaxis by means of an injection of antipneumococcic polyvalent serum administered at the same time as the first injection of diphtheria antitoxin. He thinks that it may be useful to administer also an injection of antistreptococcic polyvalent serum when there is some reason to think that the streptococcus participates or predominates in the etiology of the bronchopneumonia of patients with diphtheria.

AUTHOR'S SUMMARY.

SERUM ATTENUATION AND SERUM PROPHYLAXIS IN MEASLES. AUGUST BROSSA BOSQUE, But. Soc. catalana de pediat. **5**:96, 1932.

From 8 to 12 cc. of convalescent serum was found effective in the prevention of measles, if given early. Attenuation is advised except in unusual cases.

WATSON, Elmhurst, Ill.

TREATMENT OF MALARIA IN CHILDREN. JOSÉ M. DA ROCHA, J. de pediat., Rio de Janeiro **1**:406 (Oct.) 1934.

Da Rocha prefers the basic chloride of quinine. To children 1 year of age he gives 7 cg. per kilogram of body weight; to those 2 years of age, 8 cg., and to children of preschool age, 10 cg. They should also have iron as an accessory treatment and occasionally some form of arsenic. The quinine is given for seven days, followed by three days' rest, and then is given four days for three weeks. This is followed by four days' rest, after which it is given three days for two weeks. The final period consists of five days' rest and two days during which quinine is given.

SANFORD, Chicago.

CLINICAL NOTES ON THE USE OF ANTIALPHA VACCINE. DAVID AGUIRRE, Med. de los niños **35**:348 (Nov.) 1934.

Aguirre reports on the use of antialpha vaccine of Ferran in five hundred and seventy-eight cases of whooping cough in Guatemala. The ages of the patients ranged from 3 months to 12 years. The dose of vaccine varied from 0.25 to 1 cc. The majority of the patients had thermal reactions of elevation of temperature to 38 or 39 C. (100.4 or 102.2 F.). There were no deaths and no complications in this series. There were only three failures. Generally, immediate improvement followed the third injection.

DWYER, Kansas City, Mo.

STATISTICS ON VACCINATION AGAINST WHOOPING COUGH. HERRERO BESADO, Med. de los niños **35**;362 (Nov.) 1934.

A close relationship exists between the acid-fast bacillus of Koch and the Bordet-Gengou organism. Whooping cough, more than any other disease, is likely to be followed by tuberculosis. The author treats all patients with whooping cough with antialpha vaccine of Ferrán. Seventy per cent of children who have received antialpha vaccine are allergic to tuberculin given intradermally, while only 2 per cent of those not so treated exhibit this phenomenon. The author concludes that the antialpha vaccine of Ferrán is a good prophylactic agent for tuberculosis and almost a specific for whooping cough.

DWYER, Kansas City, Mo.

INFECTIOUS ERYTHEMA (FIFTH DISEASE). A. ROMEO LOZANO, Pediatria españ. **23**:307 (Sept.) 1934.

The author reports eleven cases of this disorder, the first series reported in the Spanish pediatric literature. The patients were observed during summer and winter months. The incubation period seemed to vary between six and seven days, but the author is under the impression that it may be even longer.

The eruption appears first about the nose and the eyelids. The face appears swollen, as though it had been struck a blow. The early redness of the rash changes to a bluish and violet-gray tinge. The eruption may also appear on the forehead and the chin. Simultaneously or a day or two later the eruption appears on the extremities and may involve the palmar and plantar surfaces. For the most part, it consists of small red spots, slightly raised and closely resembling urticarial eruptions. At times they become confluent and may assume an annular form. The type is particularly liable to occur if the eruption involves the trunk. No desquamation takes place. A normal leukocyte count or slight leukopenia is observed. Nephritis and moderate forms of arthritis may be complications but were not observed by the author in his series of cases. No treatment is required. The prognosis is uniformly good.

SCHLUTZ, Chicago.

DATA ON GERM CARRIERS AND ON ANTIDIPHTHERIA VACCINATION. SÁINZ DE LOS TERREROS, C. FORNIDES and ANDOLZ Y NOVOA, Rev. san. e hig. púb. **9**:1 (Oct.) 1934.

This is a statistical study on the morbidity and the mortality rate for diphtheria in Madrid from 1923 to 1932, inclusive. The authors conclude that the morbidity and the mortality rate for diphtheria in Madrid has been reduced in the past decade only; this is due to antidiphtheritic inoculation. Of two hundred and ninety-three school children examined, 1.7 per cent were found to be carriers of a virulent form of diphtheria and 1 per cent of an avirulent form, while 15.7 per cent harbored pseudodiphtheria bacteria. These authors are continuing the public health measures necessary to rid the country of diphtheria.

HERRON, Spokane, Wash.

PATHOLOGY AND THERAPY OF CARDIAC DISTURBANCES IN DYSENTERY OF INFANTS. PAUL VON KISS, Arch. f. Kinderh. **103**:50, 1934.

Von Kiss describes the clinical and pathologic changes of the heart in infants with dysentery. In the early stages of dysentery the cardiac changes are chiefly functional and are characterized by tachycardia and dilatation of the coronary vessels. Later in the course of the disease definite organic damage to the heart may occur, due primarily to the dysentery bacillus and its toxin and secondarily to acidosis, dehydration, changes in osmotic pressure and reduced renal function. The author believes that the infant with dysentery should be treated as one with cardiac decompensation. Rest is of the utmost importance. In the early stages large doses of digitalis and repeated small injections of physiologic solution of sodium chloride and of a 5 per cent solution of dextrose are recommended. Large amounts of blood or fluid, concentrated solution of dextrose and epinephrine are considered to be contraindicated. In the later stages of dysentery, small doses of digitalis, small doses of a 20 per cent solution of dextrose given intravenously and small blood transfusions are of greatest value.

LEMASTER, Evanston, Ill.

FOCAL REACTIONS IN DIPHTHERITIC ALLERGY. JOSEF SIEGL, Arch. f. Kinderh. **103**:223, 1934.

Three cases of focal reaction to diphtheria toxin are reported by the author. In all three cases the reaction was practically identical. Following a positive Schick reaction, Löwenstein's ointment was rubbed on the backs of the children two or three times. Later, when toxoid was injected subcutaneously, there was a marked inflammatory response at the site of the injection, a maculopapular eruption covering the area of skin where the ointment had been applied and an elevation of body temperature. Within forty-eight hours all signs of the reaction disappeared entirely.

LEMASTER, Evanston, Ill.

ERYTHEMA NODOSUM AND SCARLET FEVER. DÉNES VON MÓRITZ, Arch. f. Kinderh. **103**:227, 1934.

The author reports two cases in which erythema nodosum occurred during convalescence from scarlet fever. In both cases no roentgen evidence of tuberculosis could be demonstrated, and the Mantoux tuberculin reaction was repeatedly negative. The author believes that although most instances of erythema nodosum occur in tuberculous patients, there is occasionally a case of erythema nodosum due to allergy to the Streptococcus, such as occurred in these two patients.

LEMASTER, Evanston, Ill.

SHOULD DIPHTHERIA ANTITOXIN TREATMENT BE COMPLEMENTED BY NONSPECIFIC ANTIGEN THERAPY? ROBERT BOVERI and WERNER LOOK, Arch. f. Kinderh. **104**:1, 1934.

Boveri and Look discuss the theory concerning the beneficial effects of nonspecific protein therapy in various infectious processes. Because they had seen many patients with severe diphtheria fail to respond to treatment with antitoxin, they decided to complement the treatment with antitoxin serum with nonspecific protein therapy. For this purpose they chose to use a vaccine composed of nonpathogenic colon bacilli, given intravenously. This combined treatment was used with excellent results in eighteen cases. The plan of treatment is to use diphtheria antitoxin immediately when the diagnosis of diphtheria is made. If the patient does not respond well, the vaccine is given intravenously. In many instances the authors saw a rapid beneficial response after the administration of the vaccine, when the diphtheritic process had continued to advance following the use of antitoxin alone.

LEMASTER, Evanston, Ill.

VULVOVAGINITIS DYSENTERICA. ZOLTÁN TEVELI, Arch. f. Kinderh. **104**:69, 1935.

A 1 year old child was admitted to the clinic with acute dysentery and acute vulvovaginitis. Bacteria of the Shiga-Kruse type were cultured from the stool. The vaginal discharge yielded a pure culture of Flexner-Y dysentery bacilli. The vulvovaginitis cleared in a short time, but the child died later of the dysentery and an intercurrent respiratory infection. This case is reported because of the rarity of vulvovaginitis due to dysentery bacilli. LEMASTER, Evanston, Ill.

THE DYSENTERY EPIDEMIC OF 1933 IN BUDAPEST. JULIUS TOMÁSI, Arch. f. Kinderh. **104**:75, 1935.

In the epidemic of dysentery of the summer of 1933 in Budapest the disease was due to Shiga bacilli in a higher percentage of cases than in previous years. Of fifty infants and children with dysentery, positive cultures of dysentery bacilli were obtained for forty-seven. In 55.3 per cent the disease was due to the Flexner-Y type and in 40.4 per cent to Shiga bacilli; in 4.3 per cent of the cases both types of organisms were found. The mortality of those children with infection with the Flexner-Y bacillus was 19.2 per cent and of those with infection with the Shiga bacillus, 42.1 per cent. Agglutination reactions with the serum of the patients were of no value in diagnosis. LEMASTER, Evanston, Ill.

POSTDIPHTHERITIC PSEUDOTABES. ARNO WERNER, Deutsche med. Wchnschr. **60**:1543 (Oct. 12) 1934.

Werner describes the case of a 28 year old adult whose outstanding clinical symptoms were reflex iridoplegia and absence of the patellar reflexes.

The patient gave a history of having had severe diphtheria at the age of 12 years, with visual disturbances and partial paralysis of the lower extremities. The visual disturbances cleared up completely, and the paralysis of the legs disappeared. The past and the family history were otherwise irrelevant.

Physical examination of the patient showed vasolability, slightly enlarged thyroid glands and a slightly elevated blood pressure.

The pupils were of unequal size and irregular, without the light reflex and with a sluggish accommodation reflex. The fundi were normal; slight astigmatism was present. Both knee jerks were absent and both achilles reflexes diminished. The patient could walk well, with a slight dragging of the feet. There was no definite ataxia. The Brauch-Romberg sign was negative. There was some uncertainty in recognizing needle pricks over the upper two thirds of the inner aspects of the thighs. The blood picture was normal; the Wassermann reaction of the blood and the cerebrospinal fluid was negative. There was no increase of cells or proteins in the spinal fluid, and the result of the colloidal gold test and the normomastic were normal.

Kellner in 1922 described the first case of reflex iridoplegia following diphtheria. Werner's case is the second in the literature. The condition deserves the name pseudotabes postdiphtherica more than the condition in Kellner's case because of the presence of reflex iridoplegia, the absence of the patellar and the diminution of the achilles reflex and, finally, the "saddle" type of anesthesia.

KERESZTURI, New York.

SERUM TREATMENT AND PROTECTIVE IMMUNIZATION IN SCARLET FEVER. H. MOMMSEN, Med. Klin. **30**:1189 (Sept. 7) 1934.

Mommsen discusses serum therapy and protective inoculation against scarlet fever, without making any new contribution to the generally accepted ideas on the subject. He believes that the mild character of the scarlet fever now seen in Germany makes general protective inoculation unnecessary, particularly so long as that procedure remains in the present experimental stage.

DOOLEY, New York.

VACCINE TREATMENT OF WHOOPING COUGH. E. SAUER, Med. Klin. **30**:1195 (Sept. 7) 1934.

Sauer gave pertussis vaccine to one hundred and seven children and concluded that it was very beneficial in prophylaxis and in the early, catarrhal stages of infection, but ineffectual in the severe, convulsive stages. DOOLEY, New York.

THE EPIDEMIOLOGY OF SCARLET FEVER. S. WOLFF, Med. Klin. **30**:1529 (Nov. 16) 1934.

A family epidemic started with a typical case of scarlet fever on Dec. 31, 1933, and involved eight persons between that time and March 17, 1934. Two of the eight persons had classic scarlet fever; one had atypical scarlet fever; two had purulent otitis media, and the remaining three had simple angina. A hemolytic streptococcus was apparently the etiologic agent in each case. Study of this epidemic gives further weight to the dicta that scarlet fever is not a disease sui generis but a symptom and that the rash is a manifestation of hypersensitivity to the streptococcus. DOOLEY, New York.

VARIATIONS IN IMMUNITY IN INFECTIOUS DISEASE. GEORG MEYER ZU HÖRSTE, Monatschr. f. Kinderh. **61**:94, 1934.

The case of a child who was vaccinated successfully is reported. While the pustule was still present pneumonia developed. After recovery from the pneumonia another pustule formed on the identical site of the previous one. In other words, the pneumonia had altered the immunity to such an extent as to lead to a reinfection with the vaccinia virus. The author uses this case to illustrate the effects of one infection on immunity reactions against another. GERSTLEY, Chicago.

DIPHTHERITIC VULVOVAGINITIS. KURT OXENIUS, Monatschr. f. Kinderh. **61**:142, 1934.

A case of diphtheritic vulvovaginitis of unknown origin in a 2 year old girl is reported to remind one that the condition exists. GERSTLEY, Chicago.

ALVEOLAR ENANTHEM IN MEASLES. H. SECKEL, Monatschr. f. Kinderh. **61**:351, 1935.

In about 5 per cent of all the cases of measles studied Seckel found an acute disturbance of respiration characterized by tachypnea without real dyspnea and also without any definite pulmonary findings and without any signs of circulatory weakness. There may be slight cyanosis. The symptom comes and goes with the rash. The author considers it due to a diffuse alveolar enanthem of the lungs. Because the prognosis is so much better than in the severer complications of measles the condition should be recognized by clinicians. GERSTLEY, Chicago.

EFFICACY OF DIPHTHERIA SERUM IN EXPERIMENTS ON ANIMALS. F. VON BORMANN, München. med. Wchnschr. **81**:1455 (Sept. 21) 1934.

In the last few years the value of diphtheria serum has been questioned. Several authors have stated that it has no specific effect. The conclusions are based on the results obtained in cases of malignant diphtheria which have been prevalent in Europe in recent years. Bormann points out that malignant diphtheria is the result of a mixed infection and that the serum has no effect on the streptococci or staphylococci present. Moreover, he shows that the mortality rates in the days before serotherapy were higher than during any period since. If serum is given on the first day of the illness the mortality is dramatically reduced.

Bormann reports his results with experimental diphtheria in guinea-pigs. He infected 368 animals and gave 118 diphtheria serum and 161 plain horse serum; the remaining 89 were kept as controls. The mortality rate in the group receiving diphtheria serum was 6.8 per cent; in the second group, that receiving horse serum, it was 62.1 per cent, and in the control group it was 89.9 per cent. The specific effect of the serum containing diphtheria antitoxin is obvious.

BRAHDY, Mount Vernon, N. Y.

EPIDEMIOLOGIC SIGNIFICANCE OF "ATYPICAL" DIPHTHERIA OF THE SKIN. T. GRÜNEBERG and F. WEYRAUCH, München. med. Wchnschr. **81**:1527 (Oct. 5) 1934.

Chronic cutaneous lesions which resist the usual dermatologic therapeutics should be considered as possible lesions of diphtheria. They may not show the typical pseudomembrane but have the appearance of a moist eczema. Diphtheritic infection may be superimposed on an operative wound, a tuberculous fistula or other infection, such as impetigo. Patients with diphtheria of the skin may be the source of infection for those contracting nasal or faucial diphtheria. Several such instances are described by the authors.

BRAHDY, Mount Vernon, N. Y.

ARE THERE ANAEROBIC STRAINS OF DIPHTHERIA IN "MALIGNANT DIPHTHERIA"? W. KOLLATH, München. med. Wchnschr. **81**:1577 (Oct. 12) 1934.

Why large doses of serum fail to effect a cure in cases of malignant diphtheria is still an unsolved problem. Doskočil isolated anaerobic bacilli as well as diphtheria bacilli from twelve patients with malignant diphtheria. The fetor oris in these patients suggests the presence of anaerobic bacilli. Diphtheria bacilli may grow under anaerobic conditions; then they do not produce the usual toxin but may produce some other irritant. Kollath reports four cases of malignant diphtheria in which he was unable, during the first few days of the illness, to culture diphtheria bacilli on ordinary mediums but was able to culture them on anaerobic mediums. Later in the disease diphtheria bacilli grew on ordinary culture medium. The question arises whether in certain cases of malignant diphtheria anaerobic strains of diphtheria bacilli are present which later in the disease change into the typical toxin-forming aerobic strains.

BRAHDY, Mount Vernon, N. Y.

DOES THE PRESENCE OF DIPHTHERIA BACILLI IN THE NOSE AND AUDITORY MEATUS INVOLVE DANGER OF INFECTION FOR THE ENVIRONMENT OF THE BACILLUS CARRIER? T. HÜNERMANN, München. med. Wchnschr. **81**:1661 (Oct. 26) 1934.

Hünermann answers his question in the negative. Diphtheria bacilli can be isolated from the nasal secretions of patients with atrophic rhinitis, ozena and dry mucous membranes with crusting. The bacilli are frequently virulent. The same observations can be made in patients with chronic eczema of the auditory canal. Clinical observations indicate that these patients are not a source of infection. They are not comparable with patients who have recently recovered from an attack of acute diphtheria.

BRAHDY, Mount Vernon, N. Y.

THE PROPHYLAXIS OF DIPHTHERIA BY COMBINED IMMUNIZATION. E. KANERT, München. med. Wchnschr. **81**:1723 (Nov. 8) 1934.

The incidence of diphtheria has increased greatly during the last few years in a sanatorium for children with tuberculosis. A combination of passive and active immunization was tried to combat the increasing prevalence of the disease. Only children in whom cultures from the nose and throat were negative for diphtheria bacilli were admitted to the sanatorium. All children newly admitted received

from 500 to 1,000 units of beef diphtheria antitoxin in addition to an injection of anatoxin for active immunization. The children were protected for four weeks by the passive immunization, and when this protection began to lessen the active immunity was increased sufficiently to prevent the occurrence of diphtheria. Following this combined method of immunization the epidemic in the sanatorium stopped.

BRAHDY, Mount Vernon, N. Y.

NUMBER AND LENGTH OF VACCINATION INCISIONS AND IMMUNITY AGAINST SMALLPOX. A. GROTH and H. O. MÜNSTERER, München. med. Wchnschr. **81**: 1842 (Nov. 29) 1934.

It was formerly thought the protection against smallpox was greatest in those persons who had numerous large scars. In 1904 Cameron showed that the morbidity and mortality rates varied inversely with the number of vaccination scars which the patient had. Groth and Münsterer revaccinated more than 9,000 children on the average of ten years after their first vaccination. They studied the immunity developed from the first vaccinations in relation to the number of incisions and the size of the scars. They concluded that the best results are obtained with three incisions. Vaccination with more incisions does not aggravate the symptoms which follow the vaccination, but it does not increase the immunity. Vaccination with two incisions decreases the immunity but does not diminish the postvaccinal symptoms. Vaccination with one incision decreases the postvaccinal symptoms, but the resulting immunity is inadequate. Each incision in the first vaccination should be from 3 to 5 mm. long, and for revaccination it should be from 5 to 8 mm.

BRAHDY, Mount Vernon, N. Y.

DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF ACETONURIA IN SCARLET FEVER. A. VOSSSCHULTE and K. ZIEGLER, München. med. Wchnschr. **81**:1970 (Dec. 20) 1934.

The authors investigated the diagnostic and prognostic significance of acetonuria in one hundred and thirty-three cases of scarlet fever. Acetone was present in the urine in 75 per cent of the cases on one or more days during the first week of the disease. Its occurrence was not related to the height of the exanthem. In patients with mild symptoms and a slight rash at the onset of the disease the diagnosis is often difficult. The presence of acetonuria adds support to the diagnosis of scarlet fever in such cases. Complications were much more frequent in patients who had acetonuria than in those whose urine did not contain acetone.

BRAHDY, Mount Vernon, N. Y.

MUMPS COMPLICATED BY MENINGITIS WITH ESPECIAL REFERENCE TO THE SPINAL FLUID. G. BRAKHAGE, München. med. Wchnschr. **81**:1975 (Dec. 20) 1934.

Brakhage reports a case of mumps complicated by meningitis in a child 5 years of age. The mother and a sister were psychopathic. The symptoms of meningitis began eight days after the swelling of both parotid glands and lasted three days. The changes in the spinal fluid were typical of meningitis occurring as a complication of mumps and persisted several days after the clinical recovery. There were no sequelae.

BRAHDY, Mount Vernon, N. Y.

DIPHTHERIA ANTITOXIN IN THE BLOOD OF THE POPULATION IN A TOWN OF JAVA. JEANNE VAN DEN HOVEN VAN GENDEREN, Ztschr. f. Immunitätsforsch. u. exper. Therap. **83**:42, 1934.

The blood of 1,641 men, women and children of Bandoeng, Java, was studied by means of Römer's technic. A comparative study of the blood of the umbilical cord and of the venous blood of parturient women confirmed the known fact that the amount of diphtheria antitoxin is about equal in both. The native population

and the Chinese adults and children had a high titer of antitoxin, which was somewhat lower in women and girls. The titers were much higher than among the European and mixed population, among whom the women showed a particularly low titer.

DAVIDSOHN, Chicago [ARCH. PATH.]

DIPHTHERIA ANTITOXIN IN HUMAN COLOSTRUM AND IN MOTHER'S MILK. JEANNE VAN DEN HOVEN VAN GENDEREN, Ztschr. f. Immunitätsforsch. u. exper. Therap. **83**:54, 1934.

In the colostrum of thirty-three of forty-three women examined diphtheria antitoxin was found in quantities varying between 1/500 and 1/50 antitoxin unit per cubic centimeter. The amount was always smaller than that in the blood serum of the mother, but the two levels were distinctly related to each other. Ten days post partum the antitoxin in the milk of the mothers was either very low or entirely absent, so that, according to the author, the antitoxin in the milk of the mothers could not have been the source of the antitoxin which was found in the blood of the infants.

DAVIDSOHN, Chicago.

THE INFLUENCE OF ACID OR ALKALI ON THE ANAPHYLACTIC SHOCK. E. RENTZ and A. KAKTIN, Ztschr. f. Immunitätsforsch. u. exper. Therap. **83**:59, 1934.

Guinea-pigs were sensitized with beef serum and fed hydrochloric acid or sodium carbonate for three weeks. The acidotic animals reacted to the reinjections more severely than the alkalinized ones. The result seems to contradict clinical experience, but on closer analysis it is found to agree fully with the known facts of the relation between acute and chronic acidosis and alkalosis and the calcium metabolism.

DAVIDSOHN, Chicago [ARCH. PATH.]

THE TOXIN OF BACILLUS PERTUSSIS. E. F. TRUSCHINA and others, Ztschr. f. Immunitätsforsch. u. exper. Therap. **83**:124, 1934.

Concentrated filtrates of cultures of four strains of the Bordet-Gengou bacillus were found to be highly resistant to heat. They produced specific immune serums when injected into rabbits. Mice immunized with the toxin became resistant to fatal doses. Treatment with solution of formaldehyde changed the toxin into an antitoxin. Skin tests showed more positive reactions in persons who had never had pertussis than in those who had.

DAVIDSOHN, Chicago [ARCH. PATH.]

SPECIFIC EFFECT OF DIPHTHERIA ANTITOXIN ON ANIMALS. FELIX VON BORMANN and O. SCHEURER, Ztschr. f. Kinderh. **55**:73 (May) 1933.

The authors performed a series of experiments on guinea-pigs that were infected with conjunctival diphtheria and compared the therapeutic effect of diphtheria antitoxin with that of antitoxin-free horse serum. They found that the diphtheria antitoxin is much more effective than the antitoxin-free horse serum in counteracting the intoxication as well as in curing the disease. On the other hand, in mild infections the plain horse serum was effective but not sufficiently to protect the loss of the eye. The authors advise the use of only antitoxin for human beings.

LEVINSON, Chicago.

RECOVERY FROM AURICULAR FIBRILLATION FOLLOWING DIPHTHERIA. FRITZ JOSEPHTHAL, Wien. Arch. f. inn. Med. **26**:15, 1934.

Josephthal reports a case of auricular fibrillation following diphtheria in a child aged 4 years.

The symptoms set in two weeks after the onset of diphtheria and were ushered in with deep cyanosis, severe dyspnea, a thready pulse and a cloudy sensorium. The heart rate was 250 beats per minute, and the tones and an electrocardiogram were typical of auricular fibrillation.

The condition was treated by the intravenous injection of hypertonic solution of dextrose. Twenty cubic centimeters of a 25 per cent solution was used, and a small dosage of strophanthus was added to this amount. In the beginning this dose was given three times daily, but it was given less frequently after a week and its administration was discontinued on the eighth day. The effect of the injection was controlled by electrocardiograms made before and after the administration of the solution of dextrose.

SCHLUTZ, Chicago.

THE PERTUSSIS PROBLEM. D. GAJZÁGÓ, Népegészségügy **10**:6 (March) 1935.

This is a short summary reporting on the present stage of the problem of whooping cough from the point of view of epidemiology, bacteriology, serology and vaccination. It is shown by the statistics compiled in Hungary and the adjoining states in 1931-1932 that during these two years the number of deaths caused by pertussis in Hungary, Czechoslovakia and Bulgaria equaled the number of those caused by scarlet fever and measles together. Of the three infectious diseases just mentioned, pertussis showed the highest lethality. The same result could be obtained from the lethality and mortality data of the statistics for Budapest from 1930 to 1934. No characteristic annual curve was to be constructed of the mortality rates of the country or of Budapest. The author recommends starting the bacteriologic and serologic diagnosis of pertussis on a larger scale and as regular work. Specific treatment with vaccine and prophylactic vaccination should be used to a large extent.

GÖTTCHE, Budapest, Hungary.

RESULTS OF THE USE OF PERTUSSIS VACCINE AND THE CLINICAL PICTURE OF THE DISEASES. MAKS ROSEMAN, Pedjatrja polska **14**:86, 1934.

Rosenman used BGB vaccine made by the National Institute of Hygiene in Warsaw, with the following results:

If vaccine was given early in the disease the results were favorable in 90.15 per cent of the cases. If it was given after four weeks, the results were favorable in 20.5 per cent. This vaccine can be used with good results in either infants or children. The dose should not be very large, usually from 200,000,000 to 2,000,000,000 bacteria; otherwise, severe reactions may result. The vaccine is given every four to five days. At present it cannot be stated that pertussis vaccine is specific. To prevent reinfection every child should be isolated.

After pertussis subsides the child usually is susceptible to other diseases. This should be combated with a change of climate. Sequelae after vaccination are rare. In order to know whether this vaccination prevents anatomic changes in the lungs or prevents only complications and sequelae, the lungs should be studied by means of roentgenograms.

KRUPINSKI, Chicago.

SPOTTED FEVER IN CHILDREN. E. M. GREENBERG and E. D. PIVOVAROVA, Azov-Black Sea Kraeve Inst. Publ., 1934, p. 3.

This interesting monograph written in Russian gives the high lights of spotted fever in children as found in Russia. Apparently this disease is rare in that country and presents diagnostic difficulties, especially in young children. Variations in temperature are very wide, and the temperature usually falls with recovery on the twelfth or fifteenth day of the disease. The spots appear on the fifth to the eighth day and disappear between the ninth and the fourteenth day. Reddening of the mouth is rare and less intensive than in mature patients. There is slight anorexia, and the liver is rarely enlarged. Complications in the respiratory organs appear as late as the fifteenth day of the disease and have no decisive values as to the prognosis. The heart beats are usually slow, and the systolic pressure is usually raised at the end of the disease, while the diastolic pressure remains somewhat low.

Complications are rare in children, and the cutaneous diagnosis can be made with the toxin of Proteus X19. In most cases the subcutaneous injection of a 1:500 solution of the toxin, in a dose of about 0.33 cc., results in a red spot at the place of puncture if no spotted fever is present. If the patient has this disease no reaction will be seen. Laboratory investigations indicate that there are an increased coefficient, KCa, absence of free hydrochloric acid in the gastric secretions and a negative skin reaction to purified toxin of Proteus X19.

YAMPOLSKY, Atlanta, Ga.

PURIFICATION OF DIPHTHERIA TOXIN BY CALCIUM PHOSPHATE. STUDIES ON THE DIPHTHERIA TOXINS II. T. KOMIYAMA, J. Orient. Med. **21**:61 (Oct.) 1934.

Roux and Yersin (1889) described a method of purifying diphtheria toxin with calcium chloride, calcium and phosphate, which was later improved on by Abt (1928). Ohyama (1931), Schmidt (1932) and other investigators also tried this method among many others, but did not pursue it any further.

This principle was analyzed in detail, and some new data were found, with which this report deals. The use of phosphoric acid and sodium hydroxide is not only more convenient but also more reasonable than the use of sodium phosphate, which was recommended by Abt. Absorption of diphtheria toxin by calcium phosphate depends on the p_H of the medium in which the precipitate is formed; e. g., it is marked in the weak acid range and is nonexistent in the alkaline range. The largest percentage yield was obtained between p_H 5.3 and p_H 6, and the purest product between p_H 6.7 and p_H 6.9, so far as the Lf unit was concerned.

EDITOR'S SUMMARY.

A RAPID METHOD OF HYPERIMMUNIZATION OF HORSES AGAINST DIPHTHERIA TOXIN. K. KURAUCHI, T. KOMIYAMA and E. ANDO, J. Orient. Med. **21**:62 (Oct.) 1934.

The preparation of diphtheria antitoxin has been believed to be a task which needs long experience and a special technic. But recent advances in the study of antitoxic immunity, especially the findings by Ramon of flocculation reaction and anatoxin, the studies by Wadsworth and Wheeler, Pope and other investigators on the production of diphtheria toxin on the semisynthetic mediums and also the improvement of the method of hyperimmunization of horses against diphtheria toxin by Sordelli, Schmidt and others, have so changed the situation that one now finds no difficulty in the preparation of diphtheria antitoxin of high potency. This report deals with the method of hyperimmunization.

Eleven horses were immunized with diphtheria anatoxin according to the method described by S. Schmidt (his modification of the Sordelli method). The immunization consists in daily injections of increasing doses, the total being about from 1 to 1.5 liters, or about from 10,000 to 16,000 units, and the period of immunization extending only about one to one and one-half months. Five of these animals were immunized with infusion-free anatoxin and the other six with ordinary infusion anatoxin. After this immunization the antitoxin content of these horses was found to be 60, 400, 500, 600, 600, 675, 800, 900, 900, 1,000 and 1,125 units, respectively.

EDITOR'S SUMMARY.

STUDIES ON RAMON'S FLOCCULATION: I. THE INFLUENCE ON THE FLOCCULATION OF PHYSICO-CHEMICAL FACTORS. T. KOMIYAMA, J. Orient. Med. **21**:107 (Dec.) 1934.

The influence of heat, acid and alkali, direct sunlight and disinfectants such as phenol, solution of formaldehyde and tricresol on the diphtheria toxin and also on the diphtheria serum were studied by means of the Ramon flocculation reaction.

AUTHOR'S SUMMARY.

STUDIES ON RAMON'S FLOCCULATION: II. IS RAMON'S FLOCCULATION A SPECIFIC REACTION BETWEEN TOXIN AND ANTITOXIN? T. KOMIYAMA, J. Orient. Med. **21**:107 (Dec.) 1934.

There are some who have doubt as to the specific nature of the Ramon flocculation reaction. Komiyama has conducted some investigations in this connection. He concludes that the flocculating substance cannot so far be separated from the toxic substance and also that the Ramon flocculation is a specific reaction between diphtheria toxin and its antitoxin. AUTHOR'S SUMMARY.

STUDIES ON RAMON'S FLOCCULATION: III. PRACTICABILITY OF RAMON'S FLOCCULATION REACTION. T. KOMIYAMA, J. Orient. Med. **21**:108 (Dec.) 1934.

The practicability of Ramon's flocculation reaction was studied and the following conclusions obtained:

1. The difference between the Lf value and the Ehrlich value is smaller than that found between the Roemer value and the Ehrlich value.

2. The great difference sometimes found between the Ehrlich value and the Lf value may be due to the great variation in individual susceptibility among guinea-pigs.

3. A marked fluctuation of the antitoxin content in the blood was noticed during the course of immunization of horses, so that after the injection of antigen it is impossible to fix a day most suitable for whole bleeding.

4. Ramon flocculation may be most conveniently employed in determining the day for whole bleeding. AUTHOR'S SUMMARY.

Chronic Infections

JUVENILE PARETIC NEUROSYPHILIS STUDIES. WILLIAM C. MENNINGER, Am. J. Syph. & Neurol. **19**:88 (Jan.) 1935.

A review of the physical complications found in a study of forty-three cases of juvenile paresis from personal experience and six hundred and ten instances collected from the literature is given. All the physical complications are tabulated, regardless of whether they had a definite bearing on the congenital syphilis or not. Tables are presented to which reference may be made for this incidence.

ROYSTER, University, Va.

RELATIONSHIP BETWEEN THE PURPURA SYNDROME AND TUBERCULOSIS. P. MARTÍNEZ GARCÍA, But. Soc. catalana de pediat. **5**:125, 1932.

Five cases are reported in which a severe tuberculous disease was ushered in with one or another of the forms of purpura. The question is raised as to which was the causative factor. It is probable that the purpura was pretuberculous.

WATSON, Elmhurst, Ill.

TUBERCULOUS PERITONITIS. B. SANCHEZ SANTIAGO, Arch. de med. inf. **3**:801 (Dec.) 1934.

A clinical case is reported, with the methods taken to arrive at a diagnosis. Different forms or clinical types of tuberculous peritonitis exist, and they can change from one form to another and show characteristic findings at different times. The treatment should consist in (*a*) healing the tuberculous infection and (*b*) healing the peritoneal localized infection. SANFORD, Chicago.

A CASE OF SYPHILIS OF THE LUNG IN A CHILD TWENTY-EIGHT DAYS OLD, WITH OBSERVATIONS AT AUTOPSY. BALANZO CABOT, But. Soc. catalana de pediat. **6**:214 (July-Aug.) 1933.

The unusual features of this case were that the lung was the only organ affected and that the child lived twenty-eight days. WATSON, Elmhurst, Ill.

AN INTERESTING CLINICAL CASE OF ALPHATHERAPY. JUAN PAULÍS Y PAGÉS, Med. de los niños **35**:360 (Nov.) 1934.

In a boy, aged 18 months, tuberculosis developed after an attack of whooping cough with bronchopneumonia. Symptoms of meningo-encephalitis were followed by optic neuritis, loss of the pupillary reflex and evidence of atrophy of the optic nerve. These disturbances of the central nervous system and the results of studies of the cerebrospinal fluid indicated a severe pathologic process with destruction or degeneration of the cells and nerve fibers at the base of the brain. Treatment consisted in hypodermic administration of arsenic, phosphorus, strychnine and calcium gluconate. On the theory that the cerebral lesions were caused by tuberculosis, antialpha vaccine was used. The result was striking, and the child was restored to perfect health.

DWYER, Kansas City, Mo.

DIFFERENCE IN THE PIRQUET REACTION ON THE TRUNK AND ON THE LIMBS. HELMUT RACKWITZ, Dermat. Wchnschr. **99**:1290 (Oct. 6) 1934.

By tests in a series of cases Rackwitz shows that the Pirquet reaction is more frequently positive when the inoculation is made on the trunk (abdomen or chest) than when it is made on the arm or leg. A considerable number of persons who showed a positive Pirquet reaction on the trunk and a negative reaction on the limbs had stigmas of disturbance of the vegetative system, especially acroasphyxia.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

TUBERCULOSIS AND DEFICIENCY OF VITAMINS. N. K. BASU, Ztschr. Vitaminforsch. **3**:91, 1934.

For the prevention of tuberculosis the diet must be well balanced and contain a sufficient supply of vitamins. As a prophylactic measure the use of vitamin concentrates may be necessary. Of guinea-pigs inoculated with Bacillus tuberculosis, the mortality rate was lowest (33 per cent) in animals on a ration rich in vitamins A, B, C and D; it was 50 per cent in animals on a ration deficient in either vitamin B or vitamin C, 66 per cent in animals on a ration deficient in vitamin D and 90 per cent in animals on a ration deficient in all four vitamins.

KUGELMASS, New York City.

CAVITIES IN THE LUNGS OF CHILDREN WITH TUBERCULOSIS. A. FESTENSZTAT, Pedjatrja polska **14**:1, 1934.

Not long ago the tuberculous cavity in the lungs of children was regarded as a rarity. However, in the last few years, because of more extensive studies on tuberculosis in children, the cavity is more often encountered and recognized, even in infants. From the standpoint of diagnosis, observation was made on thirty children. The cavities were divided into three groups:

1. Cavities recognized on physical examination and proved by roentgenographic findings. The most important physical signs are bruit de pot fêlé, bronchial breathing and increased voice fremitus.

2. Cavities which it is impossible to recognize on physical examination *(cavernes muettes)* and which are found only by roentgenography.

3. Cavities recognized on physical examination but not shown on the roentgenogram. The roentgenographic signs occur much later than those on physical examination *(cavernes parlantes)*. In general there are no extraordinary signs in children with tuberculous cavities. They cough, but spitting blood is not common in children because they do not know how to raise sputum but swallow it. The duration of the existence of the cavity varies from a month to two years, as was observed in one case.

KRUPINSKI, Chicago.

THE RELATION OF THE INTRACUTANEOUS TUBERCULIN REACTION TO THE PHYSICAL CONSTITUTION OF KOREAN SCHOOL CHILDREN. JINKEI RHI and MENSHAKU TEI, Keijo J. Med. **5**:67 (Sept. 30) 1934.

For 646 Korean children (including 353 boys and 293 girls), each 12 years of age, who were attending public common schools in Keijo, measurements of height and weight and the circumference of the chest were made, and at the same time intracutaneous tuberculin tests were made.

After the boys and girls had been divided into two groups on the basis of their reactions to the tuberculin test, the average height, weight, circumference of the chest, Rohrer's index and chest-height index were computed for each group The average circumference of the chest, Rohrer's index and the chest-height index, for the two groups, can be compared, but the average height and weight present a peculiar aspect in relation to sex. While the average height for the boys with positive tuberculin reactions is markedly higher than that for boys with negative reactions, the average weights for the two groups are almost the same. On the other hand, in the case of the girls the average heights for the two groups are nearly the same, but the average weight for the girls with positive tuberculin reactions is markedly inferior to that of the girls with negative reactions.

All these facts indicate clearly that, in general, the children with the positive tuberculin reaction are, as compared with those giving the negative reaction, thin or asthenic, an observation which conformed to our expectation. In order to visualize such a relation more distinctly, scatter diagrams of the correlation between these physical measurements and indexes are constructed.

AUTHORS' SUMMARY.

IMMUNIZATION BY VACCINATION WITH THE CALMETTE-GUÉRIN BACILLUS (BCG) M. R. HEYNSIUS VAN DEN BERG, Nederl. tijdschr. v. geneesk. **78**: 4688 (Oct. 13) 1934.

During the last eight and one-half years 1,100 infants in Amsterdam, Netherlands, were vaccinated during the first ten days of life by the oral method with BCG. The results were compared with those for children used as controls. The results are also reported for 178 children past the age of 1 year and for 143 children past 2, all of whom were vaccinated directly after birth and each of whom during the first three months of life had lived with a patient suffering from open tuberculosis of the lung in whose system tubercle bacilli were found during that time. The mortality rate from tuberculosis for children aged 1 year and less was as follows: for the nonvaccinated children, 8, or 2.7 per cent, and for the children vaccinated with BCG, 5.8, or 2.9 per cent. These values do not offer sufficient proof of immunization. However, for children in the first two years of life the values were, respectively, 18, or 3.8 per cent, for the nonvaccinated children and 2.7, or 1.3 per cent, for the vaccinated children. The author is satisfied with these results, but they indicate that still a number of children vaccinated with BCG die of tuberculosis during the first two years of life. With one exception the cases just mentioned occurred only in families in which prophylaxis was bad.

VAN CREVELD, Amsterdam, Netherlands.

A NEW CATAPHORETIC SEROLOGIC REACTION FOR SYPHILIS, TESTED ON 1,147 SERUMS. L. J. DELBAERE, Nederl. tijdschr. v. geneesk. **78**:5442 (Dec. 1) 1934.

A serologic reaction is described, based on the lowered electrical charge carried by particles of antigen suspended in the serum of a person with syphilis. The amount of this decrease of charge is measured by means of the cataphoretic rate of displacement of these particles, which is compared to that of a lipoid dye that is simultaneously suspended in the serum.

By means of the results obtained with this reaction in 1,147 serums, which were at the same time submitted to the Wassermann test and two of the usual

flocculation reactions, it has been proved that this reaction is more sensitive than the very sensitive Müller reaction, whereas no reason exists to doubt its specificity.

VAN CREVELD, Amsterdam, Netherlands.

Internal Diseases

THE POSITION OF THE HEART VALVES AND THEIR RELATION TO THE ANTERIOR CHEST WALL IN LIVING SUBJECTS WITH ABNORMAL HEARTS. MERRILL C. SOSMAN and PAUL H. WOSIKA, Am. Heart J. **10**:156 (Dec.) 1934.

Although the position of the heart valves in relation to the thoracic wall is important in physical diagnosis, little is known about it, especially when the heart is enlarged. Observation of the position of the mitral and aortic valves and annulus fibrosus in the living subject is possible in instances in which calcium deposits are present in these structures. Careful roentgenologic and fluoroscopic technic is essential. A number of hearts studied in this manner revealed great variations in position of the aortic and mitral valves as the heart enlarges or otherwise changes its relation to the thoracic cavity. This is important in the interpretation of physical signs.

GIBSON, Chicago.

FACTORS CONCERNED IN CARDIAC HYPERTROPHY: A STUDY MADE AT NECROSY OF SEVENTY-NINE CASES OF RHEUMATIC HEART DISEASE. FREDERICK A. WILLIUS and HARRY L. SMITH, Am. Heart J. **10**:190 (Dec.) 1934.

Numerous hypotheses have been advanced concerning the causes of cardiac hypertrophy. In the effort to determine the major factors and their relative importance, a careful postmortem study was made of the weight of the heart in proportion to the body weight of seventy-nine rheumatic patients. The cases were grouped according to the type of valvular lesion. The greatest cardiac weight occurred in patients with aortic stenosis, the average weight being 686 Gm. In the other groups the following average weights were found: hearts of patients with aortic insufficiency, 574 Gm.; hearts of patients with multiple valvular lesions, 524 Gm.; hearts of patients with mitral stenosis and insufficiency, 469 Gm., and hearts of patients with pure mitral insufficiency, 314 Gm.

There was an outstanding correlation between the degree of the lesion and the average weight of the heart. The duration of the lesion was of less importance. Increased cardiac work imposed by the valvular defect appears to be the outstanding influence in the production of cardiac hypertrophy in patients with rheumatic heart disease, though the length of time that the heart is subjected to the lesion and the actual myocardial injury seem to be of some importance.

GIBSON, Chicago.

DIABETIC COMA IN CHILDREN. HENRY J. JOHN, Am. J. Digest. Dis. & Nutrition **1**:569 (Oct.) 1934.

In this comprehensive article John discusses the diagnosis and treatment of diabetic coma in children. The early and adequate treatment is emphasized, and a comparison of the cases of coma under the author's care with those in which treatment was given by the family physician is made. Of thirty-one children with coma under the author's care, five died. Of nineteen who were treated by the family physician, sixteen died.

MORRISON, Savannah, Ga.

THE MECHANISM OF THE INCREASED FRAGILITY OF THE ERYTHROCYTES IN CONGENITAL HEMOLYTIC JAUNDICE. RUSSELL L. HADEN, Am. J. M. Sc. **188**:441 (Oct.) 1934.

Congenital hemolytic icterus is characterized clinically by anemia, nonobstructive jaundice and enlargement of the spleen. The erythrocytes show constant small

diameter; there are an increase in the number of reticulocytes and a decreased resistance to hypotonic saline solutions. There is a direct relation between the volume (thickness index) and the fragility of the red cells, both being increased.

HENSKE, Omaha.

AORTIC STENOSIS OF INFLAMMATORY ORIGIN WITH A DIFFERENTIAL STUDY OF THE ACQUIRED OR CONGENITAL ORIGIN OF A BICUSPID AORTIC VALVE. LOUIS FAUGERES BISHOP, LOUIS FAUGERES BISHOP JR. and MAX TRUBEK, Am. J. M. Sc. **188**:506 (Oct.) 1934.

Lesions of the aortic cusps offering varying degrees of obstruction to outflowing blood have been a frequent finding. The pathologic processes observed in the distorted valves usually fall within the following etiologic groups: (1) infections, (2) arteriosclerosis, (3) congenital defect. By a method described by Lewis and Grant, involving the use of serial sections stained for elastic and connective tissue, it was possible to differentiate a congenital raphe or a fused commissure ridge in aortic valves with advanced calcification and stenosis.

HENSKE, Omaha.

SYMPATHOGONIOMA OF THE ADRENAL. H. LEBARON PETERS and BENJAMIN HORN, Am. J. M. Sc. **188**:372 (Sept.) 1934.

Sympathogonioma of the adrenal gland is a rare tumor, consisting of the most primitive sympathetic nerve cells. A case occurring in a boy aged 2 years is reported. There were metastases to the liver and retroperitoneal lymph nodes, and death occurred within five weeks after onset.

HENSKE, Omaha.

ENLARGEMENT OF THE HEART DUE TO ABNORMAL GLYCOGEN STORAGE IN VON GIERKE'S DISEASE. WILLIAM ANTOPOL, JULIUS HEILBRUNN and LESTER R. TUCHMAN, Am. J. M. Sc. **188**:354 (Sept.) 1934.

Von Gierke's disease or glycogenosis is a metabolic perversion characterized by abnormal storage of glycogen. In comparison with Gaucher's disease, in which storage of kerasin occurs preponderantly in the reticulo-endothelial system, in von Gierke's disease this system is singularly free, the parenchymatous elements being the ones chiefly involved. A case of von Gierke's disease in which the heart was markedly enlarged is reported, and the possibility of a relationship between this malady and idiopathic hypertrophy of the heart is suggested.

HENSKE, Omaha.

THE SOCIAL INCIDENCE OF RHEUMATIC HEART DISEASE: A STATISTICAL STUDY IN NEW HAVEN SCHOOL CHILDREN. JOHN R. PAUL, ELIZABETH R. HARRISON and G. K. DEFOREST, Am. J. M. Sc. **188**:301 (Sept.) 1934.

The incidence of rheumatic disease of the heart in groups of children between the ages of 5 and 18 years was studied in an attempt to determine the influence which poverty and urban environments have as predisposing factors. On the basis of 5,758 examinations, systolic murmurs, presumably rheumatic, were found to be one and a half times as prevalent among children from the poorer districts as among those from the better districts. The average incidence of rheumatic disease of the heart among pupils attending two urban public schools was about twice that recorded among pupils of a similar age group who attended suburban and rural public schools.

HENSKE, Omaha.

THE VALUE OF THE BLOOD SEDIMENTATION TEST IN THE ROUTINE MEDICAL EXAMINATION OF ADOLESCENTS AND IN CERTAIN OF THEIR DISEASES. J. ROSWELL GALLAGHER, Am. J. M. Sc. **188**:450 (Oct.) 1934.

Seven hundred and fifty blood sedimentation tests were made either by the method of Cutler or by that of Wintrobe. The rates in normal adolescent subjects

and those in patients with common cold, mumps and bronchopneumonia are reported. The desirability of including this diagnostic aid as a part of a routine medical examination is suggested, but stress is laid on the fact that the test should in no way supplant a careful physical examination.

HENSKE, Omaha.

ESTIMATION OF CARDIAC TRANSVERSE DIAMETER IN CHILDREN AND COMPARISON WITH CARDIAC AREA. WAYNE GORDON and WRIGHT ADAMS, Am. J. M. Sc. **188**:491 (Oct.) 1934.

The relations of cardiac area and cardiac transverse diameter, as measured by roentgenograms, to sitting height, height, weight and age were studied in a group of normal children. An equation is presented for the prediction of normal transverse diameter. The article is too technical—the table of symbols used in tables and equations would be needed—for further outlining. Suffice it to say that the advantage of the cardiac area over the transverse diameter as a measure of normal cardiac size appears to be greater in children than in adults.

HENSKE, Omaha.

GLYCOGEN-STORAGE DISEASE: THESAURISMOSIS GLYCOGENICA (VON GIERKE). ELEANOR M. HUMPHREYS and K. KATO, Am. J. Path. **10**:589 (Sept.) 1934.

Glycogen storage disease (thesaurismosis glycogenica, von Gierke) is a disorder occurring in infants and children; the condition is possibly familial and affects both sexes. It is characterized anatomically by organic enlargement and the storage of glycogen chiefly, but not exclusively, in the enlarged organs. Two main types have been delimited, glycogenic hepatomegaly or hepatonephromegaly and glycogenic cardiomegaly. The affected organs may attain great size and may contain glycogen in unprecedented amounts. One peculiar feature is delayed postmortem glycogenolysis, and the search for glycogen has been successful in spite of adverse circumstances and imperfect technics. In only a few instances has storage of glycogen been associated with degenerative or proliferative changes. At least in the hepatomegalic type clinical studies have seemed to point to an impairment of the mechanisms concerned in the mobilization of glycogen and the regulation of the blood sugar. Less is known of the cardiomegalic type. Humphreys and Kato present the clinical and postmortem studies in three proved cases and one probable case of cardiomegalic glycogenosis. The fibers were enlarged, vacuolated, and (in three cases) filled with glycogen. It is probable, though it was proved in only one case, that the liver and kidneys were affected similarly but to a lesser degree. In two cases the skeletal muscles showed an unusual type of vacuolar degeneration, and in one of these the vacuoles contained much glycogen. This report brings the total number of proved cases to fifteen.

AUTHORS' SUMMARY. (MOORE, New York.)

DIABETIC HYPERPYREXIA. H. E. HIMWICH, J. F. FAZIKAS, L. H. NAHUM, D. DUBOIS, L. GREENBURG and A. GILMAN, Am. J. Physiol. **110**:19 (Nov.) 1934.

Hyperpyrexia was produced in diabetic dogs through acute anhydremia. Treatment should consist in administration of fluids and not of dextrose and insulin.

NOURSE, Cleveland.

THE ANTHELMINTIC PROPERTIES OF CERTAIN ALKYL PHENOLS. PAUL D. LAMSON, HAROLD W. BROWN and PAUL D. HARWOOD, Am. J. Trop. Med. **14**:467 (Sept.) 1934.

The authors review briefly the literature on the advantages and disadvantages attending use of hexylresorcinol as an ascaricide as well as its use in infestation with hookworms. They experimented with some of the alkyl phenols, using orthoheptyl-phenol and hexyl-meta-cresol in order to determine the effectiveness as well as the ease of administration of those preparations. These alkyl phenols were found

to be less irritating to the stomach, absorbed to a greater degree and less toxic but much less effective than hexylresorcinol in the treatment of infestation with Ascaris. They were found more effective, however, against infestation with hookworm than against that with Ascaris. The authors conclude that a good drug for use against infestation with hookworm might be found among the alkyl phenols but that these preparations are less effective than hexylresorcinol for the treatment of infestation with Ascaris.

BURPEE, Augusta, Ga.

CATHARSIS IN ACUTE UPPER RESPIRATORY INFECTIONS. FRED N. MILLER, Ann. Int. Med. **3**:972 (Feb.) 1935.

In a study of 257 university students with acute respiratory infections Miller found that cathartics taken early or at the time of admission to a university infirmary had no effect in cases of acute infection of the upper portion of the respiratory tract. This was determined by the length of time the students remained in the hospital and by the maximum temperature.

READING, Galveston, Texas.

CONGENITAL OSTEOSCLEROSIS (MARBLE BONE). CARROLL M. POUNDERS, Ann. Int. Med. **8**:966 (Feb.) 1935.

Pounders reports a case of osteosclerosis in a boy aged 3½ years. He assumes that the condition is congenital because it was first noted at that age. In early life the condition is often mistaken for rickets or syphilis. The disease is rarely suspected, and the diagnosis is made by roentgen examination, which reveals the characteristic bony changes.

READING, Galveston, Texas.

THE CLINICAL IMPLICATIONS OF THE THYMUS AND STATUS THYMICO-LYMPHATICUS. A. GRAEME MITCHELL and ESTELLE W. BROWN, Ann. Int. Med. **8**:669 (Dec.) 1934.

Mitchell sets forth the substantiated facts concerning the anatomic relations, functions and physiology of the thymus gland, in an effort to answer questions relative to the symptomatology and sudden death in cases of status thymicolymphaticus and to the diagnosis of thymic enlargement.

The records of 197 patients who were examined roentgenologically were analyzed. One hundred and sixteen of these had thymic shadows that were greater than normal. The object of the study was to determine the relationship of symptoms to thymic enlargement. Biometric methods of calculation were used.

Mitchell concludes that the thymus gland can exert sufficient pressure in the thoracic inlet to produce such symptoms as dyspnea, attacks of suffocation, crowing respiration, cough and cyanosis. There is no clear association between enlargement of the thymus, pylorospasm and convulsions. The study offers no explanation for sudden death on the basis of an existing status thymicolymphaticus.

READING, Galveston, Texas.

DUODENAL ULCER IN INFANTS: REPORT OF TWO CASES. MARK S. REUBEN, Arch. Pediat. **51**:644 (Oct.) 1934.

A report of two cases of suspected duodenal ulcer occurring in infants is presented with numerous references to the literature on this subject. The diagnosis is based on the following points: (1) late onset as compared with the onset of pyloric stenosis; (2) presence of loose stools with milk residue; (3) presence of pain when food is administered; (4) presence of blood in the stool (occult blood); (5) presence of visible peristalsis and projectile vomiting in the absence of pyloric tumor; (6) early disappearance of visible peristalsis when the symptoms abate.

WADDELL JR., University, Va.

HYPERPARATHYROIDISM AND ITS RELATIONSHIP TO DISEASES OF BONE. HENRY L. JAFFE, Bull. New York Acad. Med. **10**:539 (Sept.) 1934.

The chief activity of the parathyroid gland is the production of a hormone that helps to equilibrate the calcium and phosphorus balance between the tissues and the blood. Overactvity of the parathyroid gland is synonymous with Recklinghausen's disease of bones. As yet there exists no definite proof that hyperparathyroidism is associated with other diseases of bones such as rickets, osteomalacia, osteoporosis, etc. Jaffe gives a comprehensive discussion of Recklinghausen's disease in its bearing on experimental findings in cases of hyperparathyroidism and on its distinction from other conditions of bones mistakenly attributed to overactivity of the parathyroid gland.

JAHR, Omaha.

RAPID HYPOSENSITIZATION. G. L. WALDBOTT and M. S. ASCHER, J. Allergy **6**:93 (Nov.) 1934.

1. By administration of rapidly increasing doses of antigen it is possible to reach a relatively high state of hyposensitization. This method, however, is not devoid of danger, and a cautious gaging of the doses and of the intervals between injections is indicated. The method should be used only in case of urgency.

2. Late reactions occur more commonly than with the usual method of injection of antigen.

3. The treatment can be carried out with greater advantage if several frequent initial doses are given before the dose is increased. A more rapid increase is then relatively free from danger.

4. The evidence presented by Waldbott and Ascher indicates that it is dangerous to follow the routine in dosage prescribed by Besredka for the prevention of anaphylactic shock.

AUTHORS' SUMMARY. (HOYER, Cincinnati.)

DENTISTRY IN RELATION TO DISEASES OF THE HEMATOPOIETIC SYSTEM. THOMAS F. CODY, J. Am. Dent. A. **21**:2122 (Dec.) 1934.

Cody reviews briefly the clinical manifestations in cases of hemorrhagic purpura, of the leukemias, including myelogenous and lymphatic, aleukemic leukemia, of the anemias, including pernicious anemia and aplastic anemia, and of agranulocytic angina. A review of five cases of the last disease reported in the last decade is used to emphasize the distinction made in 1933 by Bulmer between "true agranulocytic angina, for which no cause can be found, and malignant neutropenia, in which a failure of the polymorphonuclear leukocytes (granulocytes) is secondary to an obvious acute infection." The detailed report of the case of a woman aged 44 with agranulocytic angina is given.

NOYES, Chicago.

ACCIDENTAL INJURY TO THE BOWEL DURING INTRAPERITONEAL INJECTION. GENE H. KISTLER, J. Lab. & Clin. Med. **20**:155 (Nov.) 1934.

Kistler studied the intestines of two hundred and fifty animals after intraperitoneal injections had been given. In six of these animals there were definite injuries to the intestine, and in one animal death occurred as a result of acute generalized peritonitis. It is suggested that such injuries occur more frequently than is generally appreciated. The author does not discourage the use of intraperitoneal administration of fluids in children, but he recommends that extreme care be exercised in the administration. As to the technic, he advised the use of a short beveled needle of medium size with a stylus. The abdominal wall should be relaxed, and the needle should be inserted obliquely to the plane of the wall. After it has been inserted the needle should be withdrawn slightly to make sure that the point has not pierced the intestinal wall. If there is distention particular care should be used.

McMURRAY, Galveston, Texas.

HEMOGRAPHY IN DIAGNOSIS, PROGNOSIS, AND TREATMENT BASED ON 6,000 SCHILLING HEMOGRAMS. WALTER J. CROCKER and E. H. VALENTINE, J. Lab. & Clin. Med. **20**:172 (Nov.) 1934.

Crocker and Valentine give a full discussion of interpretation of blood smears and a new method of expressing the Schilling count. They conclude that such a method should supersede all other forms of differential counts, because, in their experience, this method reflects more consistently and more accurately the degree of intoxication.

McMURRAY, Galveston, Texas.

THE TREATMENT OF MUSCULAR DYSTROPHY WITH GELATIN. LEO STONE and MILTON M. ABELES, J. Nerv. & Ment. Dis. **80**:285 (Sept.) 1934.

Muscular dystrophy has long been associated with creatine metabolism, and as amino-acetic acid is the precursor of creatine, it was thought that amino-acetic acid may offer a therapeutic advantage in the treatment of various dystrophies. In this study gelatin containing from 15 to 20 per cent of amino-acetic acid was administered in daily doses of 100 Gm., and the results observed led to the following conclusions: Gelatin has some therapeutic value probably more marked in early cases of pseudohypertrophic muscular dystrophy. Although the gelatin had to be taken in large amounts there were no ill effects from it other than occasional gastric discomfort and muscular dysesthesia. The presence of sensory phenomena and even slight motor improvement in patients with conditions other than primary muscular dystrophy suggests that there may be similarities, perhaps identities, between disorders of muscle metabolism that are primary and those of neurogenic origins and that some aspects of the latter disorders may, therefore, be favorably influenced by amino-acetic acid.

JAHR, Omaha.

FOREIGN BODIES IN THE INTESTINES. CHEVALIER JACKSON and CHEVALIER L. JACKSON, M. Rec. **140**:285 (Sept. 19) 1934.

The authors give the following summary: 1. Foreign bodies that have reached the intestines require watching because of the possibility of the somewhat rare but dangerous complications. 2. The most frequent complications arise from ulcerative penetration by pins, needles, safety-pins and bones and especially from the lodgment of relatively long foreign bodies, such as hairpins, in the turns of the duodenum in children. 3. If the foreign body is radiopaque it should be watched by means of roentgenograms made daily; fluoroscopic observations alone are not sufficient. A roentgenogram should be made in the lateral as well as in the anteroposterior position. 4. If the foreign body remains in one location referable to the viscera for as long as a week abdominal section for removal is advisable, as ulceration is certain. So long as the foreign body keeps moving onward there is little or no danger. 5. If the foreign body is radioparent the abdomen should be carefully palpated. 6. No cathartics should be given. No change in the diet should be made. Normal intestinal contents and action afford best conditions for safe passage. 7. As a prophylactic measure all foreign bodies whose passage through the intestines may involve risk should, if discovered in the stomach, be removed through the mouth by gastroscopy.

WILLIAMSON, New Orleans.

PYLOROSPASM—HYPERTROPHIC PYLORIC STENOSIS. HARRY R. LITCHFIELD, M. Rec. **140**:470 (Nov. 7) 1934.

Litchfield observed several patients with pylorospasm for whom operation had been advised as the only means of relief. These patients were put on a diet consisting of a mixture of breast milk and powdered and protein milk, and in cases in which extremely fine curds were required evaporated milk was substituted for the powdered milk in the mixture. The child was given ¼ of a tablet containing phenobarbital and bellafoline, which had been crushed, mixed with ½ teaspoonful of boiled water, allowed to cool and added to the formula. This was given three

times a day. Pyloric stenosis or pylorospasm is a self-limited disease which in most cases can be cured by medical and dietetic measures. Pyloric obstruction is a common and serious condition of unknown etiology which manifests itself in the first few weeks of life. The proportions of formulas and details as to quantity, periods and manner of feeding are given. WILLIAMSON, New Orleans.

REPORT OF A CASE OF HIRSCHSPRUNG'S DISEASE. S. J. ESSENSON, M. Rec. **140**:600 (Dec. 5) 1934.

A mild case of Hirschsprung's disease occurring in a girl aged 9 years is reported. Essenson discusses the theories as to the etiology and the treatment of the disease and draws the following conclusions: 1. Hirschsprung's disease is of neurogenic origin. 2. Hypothyroidism is found in a great number of patients with Hirschsprung's disease, and thyroid medication ought to be given, especially to obese patients. 3. Extirpation of lumbar sympathetic ganglions is the best surgical procedure, if surgical intervention is found necessary. 4. Medical treatment should always be tried. WILLIAMSON, New Orleans.

ACUTE ANAPHYLACTIC SHOCK FOLLOWING INTRACUTANEOUS TEST FOR SENSITIVITY TO HORSE SERUM. HAROLD J. FREEDMAN, New England J. Med. **212**:10 (Jan. 3) 1935.

Freedman reports the case of a 6 year old boy who for a number of years had suffered from recurrent attacks of asthma and eczema. Twenty days before he came to the clinic he received an injection of diphtheria toxin-antitoxin at school. Six days later he suffered a severe attack of asthma which lasted for three days. The attack of asthma was followed in three days by a severe urticarial reaction. In order to test the patient for sensitivity to horse serum an intracutaneous injection of 0.05 cc. of horse serum was given. Two minutes after the material was introduced into the skin a large wheal formed at the site of injection and urticaria appeared on the face and body. Five minims (0.3 cc.) of epinephrine hydrochloride was injected into the left arm. Approximately one minute later the child doubled up and complained of abdominal pain. In a few seconds he became intensely cyanotic, and respirations ceased. Emergency treatment consisted in further injections of epinephrine hydrochloride subcutaneously and into the heart, application of manual artificial respiration and the use of the Drinker respirator. These measures were ineffective. The child died about eight minutes after the test was made; he had received over 1 cc. of epinephrine hydrochloride before respiration ceased. Permission for necropsy was not obtained. GENGENBACH, Denver.

REPORT OF CASE OF TORSION OF THE SPERMATIC CORD IN A BABY TEN MONTHS OLD. FRANCIS F. HENDERSON and PHILIP S. FOISIE, New England J. Med. **211**:493 (Sept. 13) 1934.

The child had a hydrocele on the right side. The parents had been advised to have this condition repaired, but they had refused, and the hydrocele had been tapped, the treatment resulting in temporary relief. About two months later the mother noticed that the patient seemed to be in pain and cried almost constantly. She also noticed a swelling in the left inguinal region. When the child was examined it was found that the left testicle was not in the scrotum and that there was a hard, tender mass in the region of the left external ring. There were no abdominal symptoms, and the bowels were said to have moved freely that morning. The patient was immediately taken to the hospital, and under ether anesthesia an incision was made over the external ring. The spermatic cord was engorged and twisted counter-clockwise one and one-half times. The testicle and epididymis were black. When the torsion was corrected hot cloths were applied to the testicle and epididymis for some time, but as no change became visible it was obvious that the blood supply of these organs was permanently cut off, and they were

amputated. After the testicle was removed a small direct hernia was noted, and the abdominal wall was firmly sutured for the repair of this condition. The patient made an uneventful recovery.

The condition is confused chiefly with strangulated hernia and acute epididymitis.

GENGENBACH, Denver.

NUTS AS BRONCHIAL FOREIGN BODIES. LYMAN G. RICHARDS and JOHN WALKER, New England J. Med. **211**:653 (Oct. 11) 1934.

A survey of the foreign bodies which have been removed from the larynx, trachea and bronchi of children admitted to the Children's Hospital in Boston during the last ten years reveals that in twenty-six instances, or 36 per cent, the foreign body was some form of nut, inadvertently inhaled while being eaten. The youngest patient was 12 months, and the oldest 4 years old, and the average age was 3¼ years.

In the series of cases reported by Richards and Walker in which nuts were removed by aspiration there is not a single case in which, when the history in any way raised a definite suspicion of foreign body, one was not found to be present. The authors express the belief that when the history does not suggest the presence of a foreign body but signs and symptoms are in the least suggestive, a diagnostic bronchoscopy should be performed.

The average interval which elapsed before the patients entered the hospital was twelve days.

There was an almost complete lack of so-called arachidic bronchitis throughout the entire series. A persistent irritative cough was likely to be present. The three most common signs were unilateral limitation of expansion of the lung and chest on the affected side, hyperresonance to percussion (so-called obstructive emphysema) and absence or great diminution of breath sounds. It is interesting to note that râles were recorded in these cases on only nine occasions. They were indicative of some suppuration or, more frequently, of a fragment of nut in the trachea.

GENGENBACH, Denver.

PATCH TESTS IN THE DETERMINATION OF ARSPHENAMINE SENSITIZATION. HARRY M. ROBINSON, South. M. J. **27**:845 (Oct.) 1934.

In a patient known to be sensitive to arsphenamine a positive patch test with neoarsphenamine is confirmatory evidence of the persistence of sensitization. Nevertheless, the patch test is of no practical value for the demonstration of sensitization to arsphenamine since it is sometimes positive in normal persons and is often negative in those known to be sensitive to arsphenamine. The decision whether arsphenamine therapy should be continued or interrupted in a patient who has suffered from a postarsphenamine dermatitis should not be based on the results of a patch test.

SCHLUTZ, Chicago.

PATHOLOGY OF SICKLE CELL ANEMIA. L. W. DIGGS and R. E. CHING, South. M. J. **27**:839 (Oct.) 1934.

According to Diggs and Ching, sickle cell anemia is practically limited to the Negro race and develops within the group of persons inheriting the sickle cell trait.

The sickle cell trait in absence of anemia is detectable in sections of tissue by the presence of sickled cells and by the congestion of the splenic pulp with dilatation of the capillaries in the region of the malpighian body.

Anatomic evidence indicates the existence of transitional stages between the sickle cell trait and severe sickle cell anemia.

The essential features of the pathologic picture of sickle cell anemia are: (*a*) sickled erythrocytes, congestion of capillaries, thrombi, infarcts and fibrosis; (*b*) hemolytic anemia with increased phagocytic activity of the reticulo-endothelial system, retention jaundice, deposits of pigment in the liver, spleen, bone marrow,

lymph nodes and kidneys, hyperplasia of the bone marrow, a regenerative blood picture and degenerative visceral changes; (*c*) other noteworthy changes in the tissues consisting in splenic congestion at an early stage of the disease followed by hemorrhage, infarction and fibrosis with formation of siderotic nodules and atrophy at a late stage of the disease, hepatomegaly with prominent Kupffer cells, congestion, pigmentation and scarring of the kidneys, cardiac enlargement, ulcers of the legs and changes in the bones.

The expectancy of life in cases of sickle cell anemia is less than 30 years. The highest incidence of death is in the first decade. Pneumonia, tuberculosis and other infections are common complications, but death may be due to the anemia alone.

SCHLUTZ, Chicago.

THE DIAGNOSIS OF BACTERIAL ALLERGY. GRAFTON TYLER BROWN, South. M. J. **27**:856 (Oct.) 1934.

Just as sensitization to foods, substances from the epidermis of animals, pollens and fungi, bacterial sensitization can be the cause of any of the allergic diseases, namely, asthma, perennial hay fever, urticaria, angioneurotic edema, eczema or migraine. Bacterial allergy in the individual case may be suspected from the history and confirmed by means of cutaneous tests with bacterial proteins, autogenous vaccines or stock vaccines.

SCHLUTZ, Chicago.

THE ROENTGENOLOGICAL DIAGNOSIS OF MECKEL'S DIVERTICULUM. GEORGE E. PFAHLER, Surg., Gynec. & Obst. **59**:929 (Dec.) 1934.

Variations in the anatomy of this anomaly, which occurs in about 2 per cent of subjects, are discussed. Two cases in boys aged respectively 7½ months and 7 years are reported.

Symptoms in children are similar to those of acute appendicitis (especially when perforation of the diverticulum has occurred), peritonitis, intestinal obstruction in general and intussusception in particular. Hemorrhage from the bowel is a frequent and important symptom. This may be observed before actual perforation independently from the surgical picture imminent on the occurrence of perforation.

In the case of the infant aged 7½ months roentgen examinations were made with the utmost care following the occurrence of hemorrhage from the bowel, because a brother of the patient had died at 1 year of age of a perforation of Meckel's diverticulum. Diverticulectomy was performed on the basis of the symptoms and of the strongly suggestive roentgen evidence. Findings at operation confirmed the diagnosis, and recovery was satisfactory.

The 7 year old boy presented symptoms of appendicitis, the existence of which was not confirmed. Repeated roentgen study following administration of barium sulfate showed evidence of active peristalsis in a pear-shaped sac above the left iliac crest. This sac did not empty itself even when the bowel was otherwise empty as shown by roentgenograms. Subsidence and nonrecurrence of the symptoms in this case made operation unnecessary.

The reports are supplemented by roentgenograms supporting the author's interpretations. It is his belief that roentgen studies of the small intestine have been generally inadequate and that in work of this type an effort to demonstrate Meckel's diverticulum more frequently should be made.

GRAVES, New York.

SUBPHRENIC ABSCESS IN CHILDREN. J. IRELAND, Surg., Gynec. & Obst. **59**:789 (Nov.) 1934.

Reports of cases of subphrenic abscess in children have been rare. Six cases are reviewed in detail. In four the abscess occurred after acute appendicitis; in one it followed lobar pneumonia, and in one it developed after rupture of a gastric ulcer in a child aged 2 years. All the abscesses were apparently intraperitoneal, and four of the six were located between the liver and diaphragm on the right side.

In three cases thoracic complications were present. Only one of the six cases terminated fatally. In one case with a favorable termination the probability was accepted that the subdiaphragmatic abscess ruptured through the diaphragm, forming a pulmonary abscess which in turn discharged through a bronchus. Cultures, which in this condition fail to show uniformity, contained colon bacillus alone, Staphylococcus aureus combined with Streptococcus mitior, Streptococcus nonhaemolyticus alone, and Streptococcus viridans.

Symptoms of subdiaphragmatic abscess often appear as a continuation of the symptoms of the primary disease. Hiccup, cough, dyspnea and pain and tenderness in the subphrenic region and sometimes edema in the lower portion of the axilla have been reported. Physical signs include those referable to empyema, with, however, the presence of râles at the base of the lung and convexity of the area of dulness upward without change of its location on change in posture. The presence of gas in the abscess cavity may give rise to separate zones of resonance comprising a region of normal pulmonary resonance above a tympanic zone of confined gas below which there is flatness due to fluid confined below the gas stratum. The heart may be displaced. Impairment of mobility of the diaphragm, which may be elevated on the affected side, may be suspected on physical examination and confirmed by roentgenograms.

Conditions which may readily be confused with subdiaphragmatic abscess by the clinician are empyema between the base of the lung and the diaphragm, abscess of the liver, infections of the retroperitoneal space and osteomyelitis of the spine.

Without surgical intervention the outcome is ordinarily fatal. In view of the comparatively low mortality rate recorded in this series in which only one of six cases proved fatal it seems probable that with early diagnosis and prompt and appropriate treatment the mortality rate may be reduced.

GRAVES, New York.

THE DIABETIC CHILD. LEA R. RIELY, Texas State J. Med. **30**:369 (Oct.) 1934.

Riely gives a rather complete summary of the history of diabetes; he mentions the theories of etiology, discusses treatment in a general way and gives the differential diagnosis of coma.

MOORE, Dallas, Texas.

CONGENITAL ABSENCE OF ONE KIDNEY WITH ASSOCIATED ACUTE POST-INFECTIOUS HEMORRHAGIC NEPHRITIS, ANURIA AND CONCOMITANT UREMIA. S. M. WELSH and W. E. BANNEN, Wisconsin M. J. **33**:664 (Sept.) 1934.

In a 2½ year old girl whose health had been good there developed acute post-infectious hemorrhagic nephritis with anuria, which was complete for five days, and uremia. The nonprotein nitrogen content of the blood rose to 127 mg. per hundred cubic centimeters of blood. All other treatment failing, decapsulation of the right kidney gave immediate relief, and the child made a complete recovery. When decapsulation was performed the left kidney was found to be absent; the right kidney was markedly larger and heavier than normal and had two ureters. The authors state that, according to Kaufmann, unilateral absence of the kidney occurs once in 2,500 cases and that there is no report of a previous case of congenital absence of the kidney associated with such conditions as were present in their patient terminating in recovery.

JANNEY, Wauwatosa, Wis.

NEPHRITIS IN INFANCY. J. BASIL RENNIE, Arch. Dis. Childhood **9**:295 (Oct.) 1934.

Ten cases of nephritis occurring in infants under 18 months are reported. Clinical and biochemical findings are given. The disease was characterized by obstinate edema and a reduction of serum proteins in every case. Seven of the cases were fatal, death being due in five, or possibly in six, either to pneumonia

or to enteritis. In one case death was due to cellulitis. The other three cases terminated in complete recovery.

The edema was ascribed in every case to a fall in the serum proteins with consequent reduction in the oncotic pressure. This was a constant finding, and the condition differed in this respect from acute nephritis as seen in older children, a fall in oncotic pressure below edema level occurring in only 14 per cent of the older children. Attempts at treatment should be directed toward causing a rise in the serum proteins as the cure is coincident with their return to normal. Spontaneous cure such as occurs in older children accounted for all the recoveries.

KELLY, Milwaukee.

GOUT AND ALEUKAEMIC LEUKAEMIA IN A BOY AGED FIVE. C. WILFRED VINING and J. G. THOMSON, Arch. Dis. Childhood **9**:277 (Oct.) 1934.

Vining and Thomson report a case of aleukemic leukemia in a boy aged 5 years with the added picture of gout. Postmortem examination revealed gouty deposits in the joints, kidneys, liver and other organs. There was leukocytic infiltration throughout the kidneys and liver. The cells were lymphocytes.

KELLY, Milwaukee.

CORONARY ENDARTERITIS IN ACUTE RHEUMATISM. A. D. FRASER, Arch. Dis. Childhood **9**:267 (Oct.) 1934.

Histologic examination was made of the coronary arteries in four patients, 8, 9, 15 and 27 years old, who died of acute rheumatism.

There were proliferation of intimal cells, followed by fibrinous exudation or necrosis, mobile cell infiltration and the appearance of the giant and multinucleated basophils which denote the presence of the virus of acute rheumatism. Usually there is marked degeneration of the internal elastic laminae and of any other elastic layers which may have formed in the intima.

Unless complete obliteration of the lumen occurs the vascular endothelium remains intact and thrombosis does not take place. An interesting feature is the occasional isolation of small luminal spaces or even the complete partition of the lumen, which in the later stages leads to the simulation of intimal vascularization or thrombus canalization. Sometimes the intimal cells, in keeping with their mesenchymal origin, reproduce layers of what appear to be smooth muscle cells around these luminal spaces, thus giving them the appearance of thick-walled vessels.

Both coronary arteries may be affected, and the involvement may be present at any part of their course, but the condition is more commonly found in the smaller branches of the left coronary artery.

KELLY, Milwaukee.

THE SEDIMENTATION RATE IN RHEUMATIC CARDITIS. C. B. PERRY, Arch. Dis. Childhood **9**:285 (Oct.) 1934.

In this study 1,043 estimations of the sedimentation rate were made on 167 children suffering from rheumatic heart disease. The conclusions based on this study were as follows: 1. Acute rheumatic carditis is always associated with a high sedimentation rate. 2. Chorea uncomplicated by carditis may be associated with a normal sedimentation rate. 3. The sedimentation rate is an accurate index of active infection in cases of rheumatic carditis. 4. While active carditis is unlikely in the presence of a normal sedimentation rate, repeated observations are essential to confirm the absence of infection in cases running a polycyclic course. 5. Subcutaneous nodules appear late in the course of the disease as judged by the sedimentation rate and may persist after complete quiescence of the disease is established. 6. With the onset of congestive cardiac failure in cases of acute rheumatic carditis the sedimentation rate returns to normal

KELLY, Milwaukee.

THE GASTRIC SECRETION IN NORMAL AND RHEUMATIC CHILDREN. J. W. OGILVIE, Arch. Dis. Childhood **9**:327 (Oct.) 1934.

In sixty children divided into groups according to age, each group representing a difference in age of three years, it was found that there was an increase in the average maximum free and total acidity with age. The p_H of the gastric juice during fasting also showed an increase with age, as did the total chlorine content of the gastric juice.

Of ninety-nine rheumatic children, 24 per cent had hyperchlorhydria, as compared with 13 per cent of the normal children. Hypochlorhydria was present in 11 per cent of the rheumatic patients, and in only 5 per cent of the normal children. In 63 per cent of the rheumatic children, as compared with 2 per cent of the normal children, the gastric secretion was within normal limits. KELLY, Milwaukee.

BONE CHANGES IN LEUKAEMIA: CLINICAL AND ROENTGENOLOGICAL. C. E. SNELLING and ALAN BROWN, Arch. Dis. Childhood **9**:315 (Oct.) 1934.

In twelve cases of lymphatic leukemia roentgenograms revealed evidence of changes in the bones at some time during the disease. These changes consisted of elevation of the periosteum in four cases while in all the cases there was evidence of rarefaction across the shaft near the epiphyseal line.

KELLY, Milwaukee.

BONE CHANGES IN LEUKAEMIA: PATHOLOGY. I. H. ERB, Arch. Dis. Childhood **9**:319 (Oct.) 1934.

The changes in bone in acute leukemia in childhood may be grouped under the following headings: infiltration, rarefaction, proliferation, degeneration and hemorrhage.

Infiltration with leukemic cells may occur in bone as it does in the liver and kidney or elsewhere and may involve the marrow cavity, haversian canals or subperiosteal region. By replacing bone marrow it may give rise to profound anemia. It is not visible on roentgen examination.

Rarefaction occurs chiefly toward the ends of the long bones but may occur anywhere along the shaft and involve both cancellous and compact bone. Spontaneous fractures may result.

Proliferation of new bone occurs underneath the periosteum following elevation of the periosteum by infiltrating leukemic cells. This new bone is demonstrable by roentgen examination, as are also the areas of rarefaction.

Degeneration of masses of leukemic cells as well as hemorrhage into the marrow cavity may occur in the course of the disease, but these changes are of little clinical significance, except for the fact that they add to the symptoms of toxemia.

KELLY, Milwaukee.

ALLERGY, METABOLISM, AND THE AUTONOMIC NERVOUS SYSTEM. C. PAGET LAPAGE, Brit. M. J. **2**:985 (Dec. 1) 1934.

Lapage gives a discussion of the subjects as outlined in the title and the following summary: "Allergy is a state of sensitization in which the system shows habit reactions to certain foreign metabolic irritants, usually protein in nature. These reactions are dermal, vascular, haemic, respiratory, digestive, renal, arthritic, cerebral, or cardiac, according to the individual and to the local irritation, whether traumatic or infective or chemical, the last being usually the production of histamine-like bodies. Allergy tends to develop in autophils who have usually inherited an excitable autonomic nervous system and irritated an unstable metabolism. Autophils may remain unsensitized, unirritated, and in good health, or may become sensitized and irritated into being autopaths." ROYSTER, University, Va.

CYST OF THE THYMUS IN A NEW-BORN BABY. M. H. FRIDJOHN, Brit. M. J. **2**:553 (Sept. 22) 1934.

Fridjohn reports a case in which a cyst of the thymus gland pressed on the aorta and was probably the cause of death.

ROYSTER, University, Va.

THE TREATMENT OF ACUTE RHEUMATISM BY STREPTOCOCCUS ANTITOXIN. JOHN EASON and W. A. R. THOMAS, Edinburgh M. J. **41**:583 (Oct.) 1934.

Eason and Thomas report observations made at the Royal Infirmary, Edinburgh, Scotland. A small group of twelve patients were treated by serum; in only one instance was treatment given by the intravenous route. In this group were two girls about 10 years old. The authors feel encouraged, especially by the results of treatment of chorea. The improvement in most cases occurred just after the appearance of the rash caused by the serum. The improvement was usually maintained. There were no deaths. Eason and Thomas suggest that all patients with acute rheumatism should be hospitalized during the period of treatment with serum because of the risk inherent in administration of serum; one of their patients one day after appearance of the rash showed cyanosis and collapse but recovered in two days, possibly from the influence of epinephrine.

NEFF, Kansas City, Mo.

COARCTATION OF THE AORTA WITH INFECTIVE ENDOCARDITIS. JAMES W. BROWN, Lancet **2**:924 (Oct. 27) 1934.

Brown reports a case of coarctation of the aorta with complicating infective endocarditis in a woman aged 30. Streptococcus viridans was recovered in cultures of the blood. Brown states that of the 200 patients with coarctation whose cases were collected by Abbott in 1927 fourteen died of bacterial endocarditis. The abnormality most frequently associated with coarctation is a bicuspid valve of the aorta, and this was present in the patient whose case is reported by Brown.

LANGMANN, New York.

HAEMOCHROMATOSIS. J. H. SHELDON, Lancet **2**:1031 (Nov. 10) 1934.

The clinical and pathologic features of hemochromatosis are reviewed. The earliest recorded onset was in a patient aged 20. The view advanced as the most reasonable explanation of hemochromatosis is that it should be classed as an inborn error of metabolism which has an overwhelming incidence in males and which in some cases is familial. The exact nature of this metabolic error is unknown, but it concerns the inner metabolism of probably all the cells of the body and shows itself in two ways: by the production of a melanin pigment in certain situations—especially in smooth muscle, connective tissues and skin—and by the formation of an iron-containing compound in nearly all the tissues. Although the error of metabolism is congenital in origin, it does not of itself produce any disturbance of health beyond initiating a process of cirrhosis in many organs—particularly the liver and pancreas—which after it has started produces its own characteristic symptoms.

LANGMANN, New York.

THE PROGNOSIS AND TREATMENT OF BRONCHITIS AND BRONCHO-PNEUMONIA IN CHILDREN. BERNARD SCHLESINGER, Practitioner **134**:50 (Jan.) 1935.

Schlesinger discusses bronchitis as it occurs in infants. Predisposing causes may be feebleness in infants with rickets, in those with congenitally weak chests and in those in whom a septic focus, such as chronically infected tonsils and adenoids, has been present for some time. Again, bronchitis in this group may

follow measles, pertussis or influenza. Also, infants in whom asthma develops later in life are subject to attacks of bronchitis.

Schlesinger expresses the belief that the treatment should have two main objectives: i. e., to maintain the patient's strength and to help eliminate the thick, sticky bronchial secretions. He warns against overmedication in infants, as digestion may be dangerously interfered with. As to prognosis, Schlesinger is of the opinion that every case of bronchitis in a young infant may be serious because of the possibility of rapid spread of the infection to the pulmonary tissue. Fairly frequent change of position is indicated in order to avoid plugging of any of the larger bronchi, which may cause areas of pulmonary collapse.

The contributory factors in bronchopneumonia are similar to those in bronchitis. In addition to the ordinary factors poor home conditions, ill ventilated rooms and malnutrition may be important causes. Treatment is discussed in detail, but stress is laid on the fact that nursing care is of prime importance. The use of the oxygen tent is believed to be of value when cyanosis is present. Specific serum therapy is not recommended. Complications may consist of gastro-enteritis, otitis media or empyema, any one of which is serious in a young child.

Age is an extremely important factor in prognosis. In a series of 134 cases the curve for mortality according to age showed the death rate for patients under 1 year to be 65 per cent. The careful observation of the course of the pulse rate, temperature and respiratory rate may also be a guide to the ultimate prognosis.

SAPPINGTON, San Francisco.

DIAPHRAGMATIC HERNIA. R. W. B. ELLIS, Proc. Roy. Soc. Med. **28**:143 (Dec.) 1934.

By permission of H. Thursfield, Ellis reports a case of diaphragmatic hernia occurring in a child aged 6½ years. The report is accompanied by roentgenograms taken after an opaque meal and by a record of the findings disclosed by the physical examination.

WILLIAMSON, New Orleans.

NEOPLASM OF LUNG (? TERATOMA). R. W. B. ELLIS, Proc. Roy. Soc. Med. **28**:145 (Dec.) 1934.

A case of neoplasm of the lung occurring in a child aged 4½ years is reported by permission of H. Thursfield. The child was well until the age of 2 years when the abdomen began to swell and frequent attacks of diarrhea occurred. When the patient was 2¾ years old she was admitted to the hospital. The abdomen was distended, and the chest was deformed, the left side being enlarged and the superficial veins distended. The left portion of the chest was dull to percussion anteriorly and posteriorly. Breath sounds were absent over the same area. The results of complete roentgen and physical examination are given in the report, which is accompanied by roentgenograms made after injection of iodized poppy-seed oil 40 per cent and by a photograph of the patient.

WILLIAMSON, New Orleans.

PRECOCIOUS GENERAL DEVELOPMENT AND OBESITY. F. PARKES WEBER, Proc. Roy. Soc. Med. **28**:149 (Dec.) 1934.

A girl aged 13½ years weighed 67.1 Kg. and showed a good deal of pubic and axillary hair. No abdominal tumor was felt. The thyroid gland was not enlarged. The pituitary fossa appeared normal as visualized by roentgen examination. Roentgenograms of the hands showed union of the epiphyses in all phalanges corresponding to that in persons of 17 years. The author expresses the belief that the obesity exhibited by the patient was of endocrine origin, but that the deviation from normal development hardly amounted to disease.

WILLIAMSON, New Orleans.

OSTEOPETROSIS (MARBLE BONES; ALBERS-SCHÖNBERG'S DISEASE; OSTEOSCLEROSIS FRAGILIS GENERALISATA; CONGENITAL OSTEOSCLEROSIS). R. W. B. ELLIS, Proc. Roy. Soc. Med. **27**:1563 (Oct.) 1934.

Osteopetrosis was first described in 1904 by Albers-Schönberg. The roentgen appearances of the bones are characteristic. The disease involves both membrane and cartilage bones. The base of the skull, the bodies of the vertebrae and the long bones are generally most affected. A full description of the roentgenograms of all affected bones is given. Parts of the skeleton unaffected by the sclerosis usually show some degree of osteoporosis. The nature of the areas of increased density observed roentgenologically has given rise to a difference of opinion, which is reflected in the number of names applied to the condition. The condition occurs in either sex and is frequently familial. The clinical features and reports of the cases of two brothers are given. The reports are accompanied by photographs of the two children and by roentgenograms. Ellis discusses the etiology fully, and he states that at present the balance of evidence appears to be definitely in favor of a parathyroid origin of the disease.

WILLIAMSON, New Orleans.

DELAYED RICKETS COEXISTING WITH CHRONIC NEPHRITIS AND GLYCOSURIA. R. DEBRÉ, J. MARIE, F. CLÉRET and R. MESSIMY, Arch. de méd. d. enf. **37**:597 (Oct.) 1934.

The authors state that it is difficult to classify the condition under consideration with any nosologic group, but in their opinion the manifestations conform in many particulars to those of the so-called "renal dwarfism" of the English school and of the "renal rickets" described by French authors. The characteristic features of these disorders are expressed in osseous deformities similar to those seen in patients with rickets but appearing long after the usual age of 18 months. Coexisting are renal alterations; at autopsy one observes typical lesions of chronic interstitial nephritis and, in some instances, congenital anomalies such as hydronephrosis, cystic disease or great dilatation of the bladder. Clinically these cases have much in common; in the earlier stage, usually between 4 and 7 years of age, there is an arrest of growth which definitely determines the dwarfism; then appear the progressive skeletal deformities; these are more pronounced in the limbs than in the thorax and affect particularly the lower extremities. There may be tumefaction of the epiphyses, incurvation of the diaphyses, genu valgum or genu recurvatum. Roentgenograms of these osseous lesions reveal intense decalcification with marked retardation of osteogenesis.

Renal symptoms are slow to appear and must be searched for with diligence. There may be polyuria followed by albuminuria and disturbances of nitrogen metabolism. In addition there is diminution of the calcium content of the blood, an increase in the phosphorus content and a varying degree of acidosis, the latter explaining the absence of tetany. Treatment is unsatisfactory, the usual remedies employed in rickets being entirely inactive. A typical case occurring in a girl aged 11 years is reported.

AMESSE, Denver.

A STUDY OF THE TYPES, COMPLICATIONS AND PROPHYLAXIS OF RHEUMATISM AMONG CHILDREN AND ADOLESCENTS IN MODERN RUSSIA. W. MARKOUSON, Arch. de méd. d. enf. **37**:705 (Dec.) 1934.

Convinced that the present knowledge of many important phases of rheumatism is wholly inadequate, the Soviet government, through its responsible medical services, has planned an exhaustive campaign against that disease, with particular stress centering about important metropolitan areas in Russia, such as Moscow, Leningrad and Kharkof. The chief objective of this study, participated in by the entire profession, is to assemble all pertinent facts to the end that a scientific basis may be assured for prophylaxis. Among the preliminary features of this great program are: (1) establishment of a method for study of the various mani-

festations of rheumatism in children and in adolescent patients, not only during the attack but also in the interim between attacks; (2) cooperation in the preparation of scientific papers and in intensive research throughout all regions, urban and rural, of the country; (3) elaboration of a unified method of offense in cases of rheumatism in young patients, and (4) education of the people, particularly of the working class, toward a wider knowledge of the dangers of rheumatism.

AMESSE, Denver.

RARE MANIFESTATIONS OF IMPERFORATE HYMEN. CARLOS SALAZAR DE SOUSA, Arch. de méd. d. enf. **37**:721 (Dec.) 1934.

This defect is practically always discovered at puberty, when the phenomena of menstruation in the adolescent girl are not accompanied by an escape of blood. According to the author there was unusual precociousness in a girl aged 25 days. She was the first-born child of a syphilitic father and an apparently normal mother. During the first five days of the postnatal period the infant was well and gained weight; then she became fretful and restless and cried continually. For forty-eight hours before admission to the hospital she voided no urine and manifested great difficulty in the passing of the stools, which were small. Catheterization produced temporary relief, but in a few hours the symptoms reappeared. The urine was withdrawn by catheterization for several days, and then consultation with the surgical division was requested.

It was discovered that the external genitals were entirely normal, with the exception of the hymenal aperture, which was absent; at that point the vagina was tense and bulging, apparently from secretions under considerable pressure. A needle was inserted and a slightly bloody fluid withdrawn: incision resulted in the escape of such a great quantity of fluid that it was feared the bladder had been invaded through a cystocele. The extraordinary quantity of this exudate in a child under 1 month of age constitutes the chief feature of the report.

AMESSE, Denver.

MALIGNANT LYMPHOGRANULOMATOSIS OF THE RELAPSING TYPE IN A GIRL AGED SIX YEARS. W. MIKULOWSKI, Arch. de méd. d. enf. **37**:725 (Dec.) 1934.

A case of Hodgkin's disease with several unusual features is reported in detail. A Polish girl aged 6 years was brought to a hospital; she had periodic attacks of fever with chills which followed an attack of measles one year before. These seizures were noted about every fifteen days; they were accompanied by severe pain in the region of the spleen and were interpreted as manifestations of malaria, but the usual therapeutic measures failed to produce relief. Examination showed an anemic, undernourished child with a petechial eruption over the lower limbs; the temperature had been 104 F. for the three days preceding hospitalization; there were no stigmas of syphilis. There was an area of dulness in the interscapular space at the base of the left lung 3 fingerbreadths in width. Puncture elicited 2 cc. of clear lymphocytic fluid. This proved to be sterile and following a subsequent puncture inoculation of guinea-pigs also gave negative results. Investigation of the circulatory apparatus revealed a loud systolic murmur without hypertrophy and venous pulsation in the neck. The spleen and the liver were moderately enlarged. The Pirquet and Mantoux tests were negative as were also the agglutination reactions to organisms of the typhoid group, the Wassermann test and cultures of the patient's blood. The hemoglobin content of the blood was 42 per cent; there were from 2,210,000 to 3,205,000 red blood cells, 2,400 leukocytes and 50,000 platelets; the bleeding time was two minutes and the clotting time ten minutes. The urine remained normal throughout the patient's three months' sojourn in the hospital. Roentgenograms disclosed moderate increase in the prehilar shadow, and further roentgen examination during the febrile crisis showed continued augmentation of the shadow in that region.

Following this attack of fever and others which succeeded at intervals of two weeks the child manifested an almost excessive euphoria; the appetite returned, the dulness at the base of the left lung and the tumefaction of the liver and spleen disappeared; there was universal amelioration, particularly in the blood picture, which became practically normal during periods of apyrexia. The third crisis was marked by the involvement of the submaxillary and the right inguinal glands. A diagnosis of malignant lymphogranulomatosis was made, and a biopsy of material from one of the submaxillary nodes confirmed this diagnosis. Treatment with roentgen radiation at intervals of five days was begun and the usual regression noted, but after the fourth exposure the patient was removed to her home, where she died two weeks later of spasm of the glottis in a paroxysm of whooping cough contracted at the hospital.

The important features of the case were the attack of measles which could have paved the way for tuberculosis, for the recurrent fever, for aseptic pleurisy, for enlargement of the hilar glands, of the liver and of the spleen, for swelling of the lymph glands, for the negative reaction to tests with tuberculin and to inoculation tests and for the exceptional leukopenia.

AMESSE, Denver.

THE TREATMENT OF BRONCHOPNEUMONIA IN INFANTS. M. SCHACHTER, J. de méd. de Paris **54**:980 (Nov. 15) 1934.

The author reports favorably on the daily use of from 20 to 25 drops of metrazol in the treatment of bronchopneumonia in infants. He was skeptical at first but obtained surprisingly good results in cases in which the prognosis seemed bad. Metrazol is a preparation containing camphor; the exact composition is not given.

LESLIE, Evanston, Ill.

INTRAVENOUS UROGRAPHY. E. PAPIN, Progrès méd., Nov. 3, 1934, p. 1706.

The advantages of intravenous urography, particularly in cases of renal tuberculosis, ureteral stone, tumors and hydronephrosis, are discussed. Neo-iopax, the sodium salt of di-iodomethane sulfonate and skiodan are thought to be the materials of choice.

LESLIE, Evanston, Ill.

OSTEOCHONDROSIS OF THE RIGHT FEMUR. JEAN VEYRASSAT, Rev. d'orthop. **21**:591 (Nov.-Dec.) 1934.

In the case reported the chondrosis was attached to an exostosis of the lower third of the femur. Veyrassat believes that the two conditions, exostosis and osteochondrosis, may be coexistent, or the chondroma may be secondary to the exostosis. The child whose case is reported had had measles in infancy. This was the only feature of importance in the history.

RYAN, Vancouver, Canada.

PRIAPISM ASSOCIATED WITH MYELOCYTIC LEUKEMIA IN A BOY AGED TEN YEARS. G. MACCIOTTA, Pediatria **42**:1093 (Sept. 1) 1934.

Macciotta reports an unusual clinical picture occurring in a boy aged 10 years. The chief complaints were a priapism of five weeks' duration associated with pain which became intensified on micturition and an induration of the perineum with redness of the scrotum, but routine examination revealed the condition to be chronic myelocytic leukemia. The spleen was markedly enlarged, and the changes in the blood were typical, showing a total red cell count of 2,400,000, a total of 464,000 white cells, 35 per cent of which were myelocytes; a hemoglobin content of 20 per cent, and 248,000 platelets. On a subsequent examination while the patient was under observation the blood picture showed: total red cells, 1,986,000; total white cells, 814,000, of which 36 per cent were myelocytes; hemoglobin content, 21 per cent, and platelets, 300,200. Blood counts made on splenic blood revealed approxi-

mately the same pictures, with a higher percentage of myeloblasts and nondifferentiated cells.

Macciotta discusses fully the etiology and pathogenisis of the condition and directs attention to the rarity of its occurrence in children. He discusses several explanations of the priapism and concludes that it was due to a thrombosis resulting from stasis associated with the rapid increase of the leukocytes.

SIGNORELLI, New Orleans.

CONTRIBUTION TO THE STUDY OF ACUTE ORCHITIS IN INFANCY: TORSION OF HYDATID OF MORGAGNI. ALFONSO GIOVANNI CHIARIELLO, Pediatria **42**:1104 (Sept. 1) 1934.

The author reports a case of intravaginal torsion of the spermatic cord in a child aged 3 years with uneventful recovery following surgical treatment. He also reports a case of complete torsion of the hydatid of Morgagni in which cure likewise followed surgical treatment.

SIGNORELLI, New Orleans.

CLINICAL CONTRIBUTION TO THE RECOGNITION AND MANAGEMENT OF LIPOID NEPHROSIS IN INFANCY. COLLA UMBERTO, Pediatria **42**:1155 (Oct. 1) 1934.

Umberto reports seven cases of lipoid nephrosis which he observed over a period of seven years in the Ospedale Maggiore di Novarra. A detailed discussion of the frequency, etiology, prognosis and treatment is given, and Umberto concludes that therapy based on the hypodermic administration of thyroid preparations in conjunction with calcium compounds represents the most effective management in cases of lipoid nephrosis.

SIGNORELLI, New Orleans.

GLUTATHIONE IN THE BLOOD OF CHILDREN WITH VARIOUS DISEASES. P. MOLTENI and G. BECCAGUTTI, Riv. di clin. pediat. **32**:1038 (Sept.) 1934.

The glutathione content of the blood of thirty-nine children with various diseases was determined according to the method of Woodward and Fry. In cases of catarrhal jaundice (13, 14 and 20 mg. per hundred cubic centimeters) and of empyema (19, 20, 21 and 24 mg.) strikingly low figures were obtained.

In cases of malnutrition (from 26 to 28 mg. per hundred cubic centimeters), of rickets (27 to 32 mg.) and of poliomyelitis (29 to 32 mg.) definitely high values were found.

The authors do not believe that in cases of other diseases the glutathione content of the blood was consistently high or low.

HIGGINS, Boston.

PAROXYSMAL TACHYCARDIA IN A CHILD AGED SEVEN YEARS. R. PEREIRAS, Arch. de med. inf. **3**:762 (Sept.) 1934.

In a 7 year old child the ectopic center of excitation shifted, giving an auricular type when the stimulus proceeded from the auricle and an infranodal one when it proceeded from the ventricle. The tachycardia was of the progressive variety. It was considered to have its origin in a silent mitral stenosis. The attacks were not relieved by digitalis.

SANFORD, Chicago.

PERIODIC ACETONEMIA IN CHILDREN. EDUARDO DE CARVALHO, Arch. de pediat., Rio de Janeiro **7**:43 (Nov.) 1934.

This condition is characterized by periodic attacks of uncontrolled vomiting, which if left untreated may persist for from five to six days. The treatment consists in withholding food by mouth, supporting the patient by intravenous injections of dextrose and administration of sedatives if necessary. Fruits are as well tolerated as foods.

SANFORD, Chicago.

SICKLE CELL ANEMIA. ALVARO SERRA DE CASTRO, J. de pediat., Rio de Janeiro **1**:427 (Nov.) 1934.

The symptoms of sickle cell anemia as noted by the author are pallor, jaundice, and enlargement of the spleen, liver and lymphatic glands. The heart also may be enlarged. There is a tendency to recurrent respiratory infections and tuberculosis. The etiology is unknown. The disease is nearly always confined to Negroes or mulattos. Rosenow has attempted to connect the condition with constitutional hemolytic icterus. The pathologic changes consist of fibrous processes in the spleen, liver and osseous marrow. The diagnosis is made by the presence of sickling of the red cells in vitro after exposure to the air for twenty-four hours. This state is reversible, and the cells return to normal. The condition is associated with an anemia of about 2,500,000 red cells and a hemoglobin content of from 40 to 50 per cent. The prognosis is not good, the average length of life being thirteen years, and seldom do any patients with sickle cell anemia live beyond 35 years of age. Treatment is not satisfactory. Antianemic measures, administration of hematopoietic stimulants, blood transfusions and splenectomy have been used. The author reports four cases, giving the results of laboratory examinations, photomicrographs, roentgenograms and the observations at autopsy in one case.

SANFORD, Chicago.

PROGNOSIS AND MANAGEMENT OF THE BLEEDING TENDENCY IN CHILDHOOD. HEINRICH LEHNDORFF, Arch. f. Kinderh. **103**:98, 1934.

Lehndorff's classification of diseases causing a tendency to bleed seems to be useful; he divides the diseases into the following groups: (1) diseases due to vitamin C deficiency; (2) purpura due to nutritional disturbances, such as celiac disease and decomposition; (3) disturbances of hereditary and familial type, such as hemophilia, pseudohemophilia, essential thrombopenia and hereditary hemorrhagic diathesis; (4) disturbances of endocrine type; (5) disturbances of infectious type; (6) disturbances of toxic type, due to chemical poisons (benzene, arsphenamine, phosphorus), autointoxication (hepatic disorders and uremia) and unknown poisons (such as in Schönlein-Henoch's purpura and purpura fulminans), and (6) purpura due to diseases of the blood such as leukemia and anemia.

The prognosis and treatment of bleeding due to the aforementioned causes are discussed.

LEMASTER, Evanston, Ill.

RELIEF PICTURES OF THE COLON IN INFANTS. KARL GEFFERTH, Arch. f. Kinderh. **103**:231, 1934.

In studies of the relief picture the colon is first completely emptied with a cleansing enema. Barium sulfate is then injected throughout the entire course of the colon. The barium is then expelled, but particles of the opaque substance remain adherent to the mucosa of the colon so that its outline and motility can be studied fluoroscopically. In these studies on infants the author noted several differences between the colon of infants and that of adults. The mucous membrane of the colon of infants is less differentiated and more smooth than that of adults. There is much less haustration in the colon of infants. The form of the colon of infants changes rapidly. The colon quickly fills with gas.

LEMASTER, Evanston, Ill.

CONGENITAL GOITER. L. VON UNTERRICHTER, Deutsche Ztschr. f. Chir. **244**:88 (Nov. 22) 1934.

In some regions of Switzerland where goiter is endemic the condition may be found in 60 per cent of the new-born. The author reviewed the material in the obstetric clinic of the University of Innsbruck. Over a period of ten years about

8,000 women were delivered of 9,750 children. Of the women 2,500 had unquestionable goiter. Of the new-born infants, excluding infants more than one month premature, 66 had unquestionable goiter. There was no significant difference in the incidence on the basis of sex as 37 of the children were girls and 29 were boys. Eighteen of the children died at or immediately after birth. In 4 cases death was due to suffocation by the goiter. With one exception the goitrous infants had mothers with goiter. The goiters in the infants tended to decrease markedly during the first month of life. The author believes that this finding corroborates Breitner's theory that the goitrous mother during pregnancy makes demands on the thyroid gland of the embryo which may undergo functional hypertrophy to such an extent that irreversible changes may take place. A somewhat analogous condition occurs in diabetic mothers during pregnancy, when their condition may be favored by the insulin secretion of the embryo. The reason why all mothers with goiter do not deliver infants with goiter probably depends to some extent on the type of maternal goiter and also perhaps on the paternal inheritance of the infant.

GLAZER, Rochester, N. Y.

THE EPIDEMIC APPEARANCE OF JAUNDICE AMONG CHILDREN IN VIENNA. B. CHOMET, Med. Klin. **30**:1428 (Oct. 26) 1934.

In the Kaiser-Franz-Josef Hospital the number of cases of catarrhal jaundice in children increased from 49 in 1932 to 130 in 1933. Chomet agrees with Wallgreen and Lindstedt in considering catarrhal jaundice to be a specific infectious disease. His records indicate that the period of incubation is from four to five weeks. Besides the usual gastro-intestinal disturbances Chomet frequently found symptoms of angina and bronchitis as the initial symptoms. Bradycardia appeared constantly, and in some children accompanying nephritis and cystitis developed. The leukocyte counts were usually diminished, the count ranging from 3,000 to 5,000. The blood sedimentation time was increased and the galactose tolerance, decreased; both of these findings were interpreted as indicating parenchymal damage to the liver.

DOOLEY, New York.

OIL OF CHENOPODIUM IN THE TREATMENT OF ASCARIS INFESTATION IN CHILDREN. SCHULTZ-SCHMIDTBORN, Med. Klin. **31**:47 (Jan. 11) 1935.

The author pleads for the consideration of infestation with Ascaris in the differential diagnosis in cases of vague abdominal pain and of diarrhea in children. He thinks that in certain patients operated on for appendicitis the symptoms are really due to ascariasis. As a result of his experience with several hundred patients he recommends administration of oil of Chenopodium and insists that it be given together with castor oil if toxic symptoms are to be avoided.

DOOLEY, New York.

TISSUE REACTIONS IN PNEUMONIA. J. BARLA-SZABÓ, Monatschr. f. Kinderh. **61**:101, 1934.

In reports of previous experiments with tissue reactions induced by plasters of cantharides according to the technic of Kaufmann Barla-Szabó has written of the differences in reactions obtained during the course of lobar pneumonia and bronchopneumonia. In cases of lobar pneumonia the reaction was more or less specific and typical or, as Barla-Szabó describes it, allergic, being first anergic and then hyperergic. In cases of bronchopneumonia the reactions were variable and indefinite. The present study deals with the tissue reactions during complications of these diseases, such as empyema. The same rule holds true. The tissue reaction in cases of bronchopneumonia is labile, probably as a result of the frequent change of immunologic conditions.

GERSTLEY, Chicago.

ADRENAL TUMORS IN CHILDREN. FRIEDRICH ECKARDT, Monatschr. f. Kinderh. **61**:127, 1934.

Eckardt gives a review of the literature and reports a case including the pathologic observations of one of the rarer types of tumor originating in the sympathetic nerve tissue of the adrenal. The first symptoms consisted of pain and weakness in the extremities (this was subsequently proved to be due to bony involvement) suggesting poliomyelitis, then followed a febrile period in which the diagnosis of typhoid or endocarditis was considered. Because of progressive weakness, anemia and decided changes in the blood, roentgenograms of the entire skeletal system were made; these revealed the adrenal tumor as well as involvement of practically all the bones.

GERSTLEY, Chicago.

THE SERUM TREATMENT OF PNEUMONIA. H. BECKER, München. med. Wchnschr. **81**:1487 (Sept. 28) 1934.

Becker reports his observations in 180 cases of pneumonia. Serotherapy was used in 70 per cent of the cases. The mortality rate in cases of pneumonia due to pneumococci of type I was reduced from 20 to 8.3 per cent by the use of serum. Almost equally good results were obtained by the use of serum in cases of pneumonia due to pneumococci of type II in which the mortality rate was reduced from 30 to 15 per cent. The effectiveness of serotherapy depends on early administration and on the use of monovalent serum. In cases of pneumonia classified as type III or group IV no improvement followed the use of serum. In six cases of pneumococcemia serum did not prevent a fatal outcome. Becker advises administration of large doses of serum intravenously in such cases.

As a result of his observations Becker states that all hospitals should be equipped with facilities for typing pneumococci or have suitable facilities easily available. Polyvalent serum may be used before the type is determined or in cases belonging to group IV. The use of monovalent serum in pneumonia due to pneumococci of types I and II is essential. The use of quinine seems helpful.

BRAHDY, Mount Vernon, N. Y.

LEUKOPENIA UNDER PHYSIOLOGIC AND PATHOLOGIC CONDITIONS. ULRICH STRASSER, Wien. Arch. f. inn. Med. **25**:283 (Oct.) 1934.

Strasser points out that the normal leukocyte count is functionally sufficient for all purposes of the organism. It may even represent an excess. A person may remain clinically well and have the capacity of doing work with a leukocyte count reduced to one sixth of the normal figure, and with such a reduced count even severe pathologic processes can be overcome.

Strasser is of the opinion that in most diseases one is not dealing with infections of any particular virulence but rather with pathologic processes of comparatively low virulence. The severe picture of sepsis occurs only if processes are present which prevent maturation of the myeloid cells at their place of origin and formation. It is conceivable that frequent recurring infections preceding the sepsis may damage the bone marrow.

All persons showing marked leukopenia are not necessarily easily subject to deleterious effects of infection. The author concludes that although the leukocytes are an extremely important defense mechanism they are not the only defense mechanism against bacterial infections.

SCHLUTZ, Chicago.

THE EOSINOPHIL PROBLEM. HUGO KRASSO, Wien. Arch. f. inn. Med. **26**:55, 1934.

Krasso contends that the fundamental condition for the development of eosinophilia rests potentially in the capacity of the eosinophil centers in the bone marrow to react. Intermediary metabolic products which possibly may be developed pathologically produce the eosinophilia through their effect on these eosinophil centers.

SCHLUTZ, Chicago.

THE PATHOLOGIC CHANGES IN THE SALIVARY SECRETION IN DIABETIC CHILDREN. N. R. CHASTIN, Sovet. pediat., no. 1, 1934, p. 39.

In diabetic children the salivary secretion is altered. The nutritive substances which contain carbohydrates (for example, bread) provoke a secretion greater than that induced by nutritive substances containing acids. The opposite reaction is observed in normal persons. In the period of convalescence the normal state of salivary secretion is reestablished. Chastin explains these findings by the variation in excitability of the center of nutrition under the influence of different components in the nourishment. The saliva of diabetic infants contains negligible quantities of sugar (from 13 to 20 mg. per hundred cubic centimeters). After the disappearance of hyperglycemia under treatment with insulin the secretion of sugar in the saliva ceases.

SEMENENKO-MCKHANN, Boston.

REFRACTOMETRY OF THE BLOOD DURING RHEUMATIC DISEASES IN CHILDREN. P. C. MODERATOV, Sovet. pediat., no. 1, 1934, p. 30.

Thirty-five children between the ages of 6 and 11 years and one patient aged 21 were studied by Moderatov. A high percentage of total protein usually indicated a favorable course of the disease. In the patients in whom the prognosis was favorable there was less variation in the protein fractions and those fractions were nearer to normal. In rheumatic children the fibrinogen content showed an increase associated with a decrease in the globulin. Improvement of the rheumatic condition was followed by a decrease in the fibrinogen and albumin and an increase in the globulin. So long as the normal ratio between the globulin and the albumin is not established the condition of the rheumatic patient cannot be considered improved. The condition of blood proteins during attacks of rheumatic fever seems to favor the theory that the disease is due to the slow and prolonged action of an organism or virus.

SEMENENKO-MCKHANN, Boston.

CLASSIFICATION OF DISEASE DUE TO LEAD IN INFANTS. M. KASAHARA and H. HIROSHIMA, J. Pediat. (Tokyo), no. 415, Dec. 20, 1934, p. 1838.

The authors propose the following classification of diseases due to lead, as occurring in infants, according to the symptoms: (1) anemic type; (2) encephalitic type (meningismus due to lead); (3) hydrocephalic type; (4) pseudorachitic type; (5) paralytic type; (6) convulsive type (eclampsia due to lead); (7) gastro-enteric hepatic type (jaundice due to lead); (8) retardatory type (causing retardation in physical and mental development); (9) motor type.

KATO, Chicago.

STUDIES ON CAPILLARY RESISTANCE. P. SCHULTZER, Acta med. Scandinav. **83**:544 and 555 (Oct. 17) 1934.

Patients with peptic ulcer were put on a diet which was deficient in vitamin C. In one third of the patients who had normal capillary resistance on admission a lowered capillary resistance developed.

On admission the patients with ulcer did not show a lowered capillary resistance more frequently than other patients entering the hospital; this finding speaks against deficiency in vitamin C as an etiologic factor in cases of peptic ulcer. The lowered capillary resistance did not return to normal until the diet was changed, but when addition of tablets of spinach concentrate was the only change made in the diet the capillary resistance returned to normal.

KAJDI, Baltimore.

DETERMINATION OF THE CALCIUM CONTENT OF THE BONES IN VIVO. A. W. ENDTZ, Maandschr. v. kindergeneesk. **4**:7 (Oct.) 1934.

The arrangement and use of the Pulfrich step photometer adapted to measure roentgenograms of bones in vivo are described; the theoretical basis of the method is discussed. The error of the method is discussed and found to be caused by

irregularities of the film. The author gives a number of values obtained by this method for the calcium content of the bones in children; the figures show that there exists a reliable mean value. Furthermore, he gives the results obtained in two cases of rickets as a demonstration of the practicability of the method.

VAN CREVELD, Amsterdam, Netherlands.

Nervous Diseases

ALTERATIONS IN MINERAL CONSTITUENTS OF ANTERIOR HORN CELLS IN EXPERIMENTAL POLIOMYELITIS. W. E. PATTON, Am. J. Path. **10**:615 (Sept.) 1934.

The nerve cells of the spinal cord have been studied by the technic of microincineration in cases of experimental poliomyelitis in monkeys. At first, there are swelling of the cell and diminution of its inorganic content, then granulation of the cell, which is correlated with hypermineralization, and necrosis with reduction again in the amount of mineral constituents.

MOORE, New York.

CLINICO-PATHOLOGIC OBSERVATIONS ON INFANTILE PARALYSIS: REPORT OF ONE HUNDRED AND TWENTY-FIVE ACUTE CASES WITH SPECIAL REFERENCE TO THE THERAPEUTIC USE OF CONVALESCENT AND ADULT BLOOD TRANSFUSIONS: THE POSSIBLE RELATION OF BLOOD GROUP TO THE SEVERITY OF THE DISEASE. D. MURRAY COWIE, J. P. PARSONS and K. LOWENBERG, Ann. Int. Med. **8**:521 (Nov.) 1934.

Cowie and his associates report the results of treatment in one hundred and twenty-five cases of acute anterior poliomyelitis which occurred in epidemic form during 1931. Eighty-one patients were observed in the systemic or preparalytic stage and forty-four in the paralytic stage.

Treatment consisted in the injection of from 20 to 30 cc. of serum from convalescent patients intravenously and from 20 to 50 cc. intramuscularly and the intravenous transfusion of from 100 to 200 cc. of whole blood from convalescent patients or from adults. A few patients were given convalescent serum intraspinally. In 96 per cent of the cases of the preparalytic stage the patient escaped paralysis, and in the three cases in which paralysis was shown the involvement was slight and subsequently disappeared. In the group of twenty-seven patients treated by immunization after the appearance of the paralysis, three patients completely recovered, and six were definitely improved, making a total of nine patients, or 33.3 per cent, who showed definite improvement, as compared with a group of seventeen patients with paralysis receiving no serum therapy, 11.6 per cent of whom showed improvement and 86.6 per cent marked residual paralysis with little or no improvement.

Intravenous injections of dextrose, in solutions of from 20 to 50 per cent, were used in fifteen cases for the relief of headache, pain, muscular tenderness and bulbar symptoms. The authors were impressed with the effects of this therapy. Two patients showing bulbar symptoms who received dextrose intravenously survived.

The relationship between blood groups and the severity of the disease is discussed. The greatest number of cases of the mild or preparalytic stage occurred in persons belonging to groups III and IV (77 per cent), while severe poliomyelitis in the paralytic stage occurred in persons of groups I and II (57 per cent).

READING, Galveston, Texas.

RHINO-ENCEPHALOCELE. JEFFERSON BROWDER and J. ARNOLD DE VEER, Arch. Path. **18**:646 (Nov.) 1934.

A case of rhino-encephalocele in a new-born infant is reported. The meningoencephalocele consisted of sclerotic tissue extending from the frontal lobes through a bony defect of the nose. The olfactory lobes, tracts and striae were absent.

Subependymal nodules were scattered throughout the ventricular system. The interventricular septum of the heart was patent. The authors interpret the encephalocele as a developmental anomaly of the rhinencephalon. The presence of certain features characteristic of tuberous sclerosis suggested a genetic relationship between the two processes.

LeMaster, Evanston, Ill.

Child Psychology. Philip S. Potter, Arch. Pediat. **51**:547 (Sept.) 1934.

This article does not lend itself to profitable abstracting.

Waddell Jr., University, Va.

The Absence of Deteriorating Effects of Bromides in Epilepsy. H. A. Paskind, J. A. M. A. **103**:100 (July 14) 1934.

Most authorities state that while bromides are efficient in the eradication or amelioration of the seizures in epilepsy, their use is dangerous because they sometimes produce mental deterioration. The mental condition of from 3 to 5.5 per cent of fifty-four patients who had taken sufficient doses of bromides to affect the seizures for from one to seventeen years showed deterioration. The occurrence of deterioration in this group of more adequately treated patients was less than in a larger group of less adequately treated persons. Misleading statements in the literature regarding the adverse effects of bromides in cases of epilepsy are due to the failure to distinguish between intoxication and deterioration, the use of the drug in cases in which deterioration was destined to occur and the chance occurrence in insane or neurotic patients with epilepsy treated with bromides of the disorders of behavior that appear even when bromides are not given.

Bonar, Salt Lake City.

The Encephalitis Problem. J. B. Neal, J. A. M. A. **103**:725 (Sept. 8) 1934.

Encephalitis presents many problems which are practically impossible to solve satisfactorily at present. The disease is not new. Why it lies dormant for years to break out again is not known. Nor is its relationship to other types of acute infection of the central nervous system understood. It is generally believed that the disease is due to a neurotropic, herpes-like filtrable virus of which several strains have been isolated and propagated. These strains are not identical in their various relationships. The occurrence of encephalitis following vaccination and acute infections raises many questions regarding changes in the properties of vaccine virus and measles virus which so far are unanswerable. In respect to treatment the author is optimistic, believing that effective methods of treatment will be developed when more definite knowledge of the etiologic agent is gained. While it is not possible to think that acute epidemic encephalitis is caused at all times by the same virus, if a particular virus can be identified by serologic tests, it should be possible to raise the resistance of the patient to the disease and the development of the chronic stage by active immunization. If the chronic stage, the mechanism of the development of which is not known, is reached its further progress may be halted by active immunization. The best method of treatment found by the Matheson Commission is active immunization against the neurotropic herpes-like virus. Hyperimmune rabbit serum has been of value in a small series of cases. Another problem, that of hospitalization of the many sufferers from this disease, must receive serious consideration.

Bonar, Salt Lake City.

Epidemiology of Epidemic Encephalitis, St. Louis Type. J. P. Leake, E. K. Musson and H. D. Chope, J. A. M. A. **103**:728 (Sept. 8) 1934.

The form of the disease in this epidemic simulated type B of the 1924 outbreak in Japan and was nearly identical with the type in the outbreak in Paris, Ill., in 1933. The number of cases for the whole area was 100 per hundred thousand. For St. Louis it was 69 per hundred thousand and for the county 212. Color

or race was not an epidemiologic factor. Both the incidence and the fatality rate were strikingly increased with age. The incubation period varied between nine and fourteen days, with possibly wider limits. The occurrence of several cases in the same family was rare, as were cases of obvious contagion between patients. The spread between communities was probably by contagion from one human being to another, but individual susceptibility appeared to be a more important factor. In its typical form the disease appeared to be limited to the warm season. The results of entomologic experiments with the mosquito as a possible vector were negative. Similarly, water and milk supplies could not be incriminated.

BONAR, Salt Lake City.

EPHEDRINE SULPHATE IN THE TREATMENT OF THE BULBAR TYPE OF POLIOMYELITIS. JOHN FITCH LANDON, J. Pediat. **5**:29 (July) 1934.

In sixty-six cases of bulbar poliomyelitis treatment with ephedrine was employed intrathecally, while in one hundred and eleven similar cases there was no treatment. No beneficial effect from the use of ephedrine could be seen from the values for the mortality or the extent of paralysis. Cisternal puncture in cases of bulbar poliomyelitis is considered dangerous.

LEMASTER, Evanston, Ill.

THE OCCURRENCE OF CATALEPTIC PHENOMENA IN CHILDREN. LEO KANNER, J. Pediat. **5**:330 (Sept.) 1934.

The literature on catalepsy in children is reviewed, and six cases occurring in the Harriet Lane Home for Invalid Children, Baltimore, are reported. Four of the children were mentally retarded. In all the cases catalepsy occurred during the course of infections or toxic conditions (otitis media, measles, mumps, typhoid fever, lead encephalitis, rheumatic heart disease and chronic dysentery).

LEMASTER, Evanston, Ill.

LOW CALCIUM TETANY IN THE NEWBORN. JACOB L. ROTHSTEIN, J. Pediat. **5**:341 (Sept.) 1934.

A case of tetany due to low calcium intake in an infant 17 days old is reported and the literature on the subject reviewed. The infant was born of a mother suffering from preeclampsia and weighed 4 pounds and 4 ounces (1,927.8 Gm.) at birth. By the end of the second week of life the infant weighed 12 ounces (340.19 Gm.) more than at birth in spite of continual fever, which at times was as high as 105 and 106 F. On the thirteenth day convulsive twitchings of the face occurred for a few minutes, and on the seventeenth day generalized convulsive seizures appeared. Calcium gluconate was administered, and thirty-six hours later the determination of the calcium content of the blood showed 7.4 mg. per hundred cubic centimeters of serum. The infant rapidly improved.

LEMASTER, Evanston, Ill.

MONGOLOID IMBECILITY IN THE MONGOLIAN RACES. LEWIS K. SWEET, J. Pediat. **5**:352 (Sept.) 1934.

The author reports two clearcut cases of mongoloid idiocy in Chinese children. There are now in the literature reports of six definite instances of mongolism in Chinese children and of more than sixty in Japanese children.

LEMASTER, Evanston, Ill.

PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY. HOWARD B. METTEL, J. Pediat. **5**:359 (Sept.) 1934.

This is the second report of the author on his studies on fourteen children with pseudohypertrophic muscular dystrophy treated with amino-acetic acid. No striking therapeutic effects were observed. It is thought that amino-acetic acid may be

of benefit in the early stage but that it is of little value in the advanced stage. It is the opinion of the author that something else must be given with amino-acetic acid to create the storage of creatine in the muscle tissue. The author also briefly discusses the use of other preparations, such as thyroid extract, estrogenic hormone, insulin and various drugs.

LEMASTER, Evanston, Ill.

THE TREATMENT OF CHOREA. T. DUCKETT JONES, M. Clin. North America **18**:1081 (Jan.) 1935.

Although he admits that Sydenham's chorea is a phase of the rheumatic fever syndrome, Jones, on the basis of his observations, does not believe that it has the serious prognostic significance in regard to damage of the heart that is attached to fever, polyarthritis and other manifestations of the disease. Of 482 patients who had chorea only 51 died during a period of eight years. In a comparable number (518) of subjects with uncomplicated rheumatic fever, there were 166 deaths. An interesting fact is that death in all the 51 cases in the first group was due to rheumatic fever without manifestations of chorea during the terminal episode. In cases of simple chorea such evidences of rheumatic infection as fever and increase in the pulse rate, white cell count and red cell sedimentation rate are rarely found. Of a group of 318 patients with this condition observed for a period of eight years, 130 have remained free from other manifestations of rheumatic fever, and in only 3 per cent of these has cardiac disease developed. In the 184 remaining members of this group rheumatic fever subsequently developed, with involvement of the heart in 80 per cent of the cases.

Jones failed to observe any striking effect on the severity or continuation of chorea following the use of such therapeutic agents as barbital, salicylates, stramonium, phenylethylhydantoin or polyvalent streptococcus vaccine. He has not been impressed with the value of typhoid-paratyphoid vaccine, and he advises caution in its use. The emotional and psychologic reactions of the patient are of great importance and should be controlled as far as possible. Isolation, quiet and rest in bed are probably the most valuable general measures in treatment.

EUGENE SMITH, Ogden, Utah.

RECENT ADVANCE IN THE TREATMENT OF EPIDEMIC ENCEPHALITIS. JOSEPHINE B. NEAL, New York State J. Med. **34**:707 (Aug. 15) 1934.

The writer is the executive secretary of the William J. Matheson Commission for Encephalitis Research. She reports her experiences in the treatment of encephalitis. The Gay hyperimmune rabbit brain vaccine was used in a number of cases and gave better results than the Rosenow serum. The use of a hypertonic solution of dextrose intravenously and spinal puncture also receive favorable mention. "Finding a cure for epidemic encephalitis is one of the most challenging problems that confronts the medical profession."

AIKMAN, Rochester, N. Y.

THE DIAGNOSIS AND TREATMENT OF ACUTE POLIOMYELITIS. J. L. BLANTON, West Virginia M. J. **30**:403 (Sept.) 1934.

This article presents a rather complete and comprehensive review of the symptoms, course and treatment of acute poliomyelitis.

The different types of the disease are illustrated by case histories.

No especially new or unusual observation is claimed by the author.

SHAWKEY, Charleston, W. Va.

PROGRESSIVE PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY. ATHEY R. LUTZ, West Virginia M. J. **30**:463 (Oct.) 1934.

The author reviews one hundred and eight cases from the literature and adds twelve cases in which a "recent method" was used in treatment at the Huntington Orthopedic Hospital.

The condition is only a phase of the muscular dystrophies and not a clinical entity.

The etiology of the disease is unknown. Ninety-two per cent of the cases occur before the seventh year of life.

The treatment used by the author is that introduced in 1930 by Kuré and Okinaka and consists of the daily intramuscular injection of from 0.2 to 0.3 cc. of a solution containing one part of a 1 per cent solution of pilocarpine hydrochloride and two parts of a 0.1 per cent solution of epinephrine hydrochloride.

From six to eight weeks constitute the period of a course of treatment.

Usually in from two to four months the disease begins to progress again, and another course of treatment is instituted.

These treatments were supplemented by physical therapy.

Marked improvement was shown in every case, but whether any patient will be permanently cured remains to be seen. SHAWKEY, Charleston, W. Va.

AUTARCEOLOGY OF POLIOMYELITIS. W. LLOYD AYCOCK, West Virginia M. J. **30**:481 (Nov.) 1934.

The spread of poliomyelitis is worldwide. A large proportion of persons in the population have harbored the virus of the disease, even without symptoms.

The paralytic disease caused by this virus varies in different regions; it is limited in extent and appears to be selective.

Autarcesiologic factors in the host rather than exposure to the disease seem to determine the occurrence of poliomyelitis, but the nature of autarcesiologic resistance is unknown.

There is evidence of familial susceptibility to poliomyelitis.

The occurrence of poliomyelitis in a brother or sister of a patient having the disease in former years is striking. The author collected twenty-nine such instances in recent years. Two persons in a family were widely separated in infancy, and they never met again, yet both had poliomyelitis at different times and in different places.

Recurrence of poliomyelitis in an individual is rare, but the author collected eight such instances. Fifteen cases have been recorded in children whose parents had the disease in childhood.

Two hundred and twenty-two cases are recorded in relatives not living in the same homes or having social contact, who contracted poliomyelitis at different times and in different places. The article includes charts showing these relationships.

Diseased tonsils seem not to predispose a person to poliomyelitis.

Statistics show no reason for closing schools because of the existence of poliomyelitis in the community.

That "the child looks sicker than he ought to" is a diagnostic point of great value, as is the posture in which the child leans back braced on the hands when placed in a sitting position. SHAWKEY, Charleston, W. Va.

EPILEPSY FROM A PEDIATRIC POINT OF VIEW. W. S. LAURIE, M. J. Australia **2**:286 (Sept. 1) 1934.

The author believes that there is but one underlying pathologic condition responsible for epilepsy and that this is a developmental or less often an acquired disturbance or deficiency of neuronic associations. All the other factors act simply as excitants.

As Kinnier Wilson has stated, the positive features of epilepsy cannot be due to destruction of motor cells but must arise from irritation of these cells or from release of inhibitory influences. Hence, degenerative changes observed at autopsy are probably due to the same toxic influences that produce epilepsy and are not per se the cause of convulsions. The author regards the distribution and regulation of sensory impulses as functions of the synaptic relations of the brain cells

as a whole. He thinks that too much has been made of the positive phenomena of epilepsy and that the aura and similar symptoms are better explained by disturbances in the synaptic relations.

The three important anatomicophysiologic factors are as follows: (1) At birth almost all the neurons are present, but their axons are incompletely medullated and they are hence functionally incomplete. (2) Inhibition is still poorly developed. (3) There are rapid growth of the brain and rapid and irregular medullation of neuraxons. Hence, the association and coordination of cerebral functions are the important factors. Convulsions may be produced by emotional shock as well as by toxins.

The clinical aspects of epilepsy are explainable only if one can conceive of a condition of neuronic insufficiency, either a developmental defect arising from an antenatal influence or one in early infancy or a lesion which produces the infantile type of cerebral reaction.

The author states that the etiologic factors in his cases were as follows: heredity 5 per cent, trauma 5 per cent, acute infections 3 per cent, congenital mental defects 8 per cent, defects of feeding in infancy and rickets 14 per cent and congenital syphilis 4 per cent. No cause was found in 20 per cent of the cases. Epilepsy followed convulsions in infancy in 14 per cent of the instances.

In the treatment prevention of nutritional disturbances of infancy is stressed. Feeding an actual ketogenic diet or one low in carbohydrates is advised. The bromides have been replaced by the barbiturates as the most reliable means of medication.

TENNEY, Madison, Wis.

PURULENT ASEPTIC MENINGITIS. R. TURQUETY, Paris méd. **2**:325 (Oct. 27) 1934.

During the course of what appeared to be a grippal infection, signs of meningeal irritation, stiffness of the neck and vomiting developed on the fifth day in a child of 18 months. The ear drums, which were slightly injected, were punctured, but no pus was obtained. The meningeal signs increased, and on the seventh day lumbar puncture yielded a cloudy fluid, which contained numerous polymorphonuclear cells of altered state, an increased amount of protein and a slightly decreased percentage of sugar. No organisms were found, and cultures made at that time and on three subsequent occasions were sterile. The child began to recover on the twenty-fourth day of the illness and has shown no sequelae. The author reviews the literature on aseptic meningitis.

LESLIE, Evanston, Ill.

TETANY IN INFANTS AGED LESS THAN THREE MONTHS. E. GORTER and J. J. DE DOES, Rev. franç. de pédiat. **10**:709, 1934.

Seven cases of tetany in infants aged less than 3 months are reported. In all the cases a low calcium content of the blood was shown. Treatment consisted in a diet of human milk, calcium therapy and the administration of cod liver oil and parathyroid extracts.

LESLIE, Evanston, Ill.

TREATMENT OF SPASTIC PARALYSES. J. DELCHEF and G. ROUDIL, Rev. d'orthop. **21**:434 (Sept.) 1934.

The authors discuss the spastic paraplegias thoroughly, starting with the anatomicophysiopathologic description of the conditions and terminating with a consideration of treatment. The article has special reference to Little's syndrome and the encephalopathies.

Treatment is complex. There is no specific therapy, but since syphilis is always present, antisyphilitic treatment should be carried out. When hematoma occurs and can be localized, puncture and drainage are advised, either through a trephine opening or through the fontanel. Orthopedic treatment and physical therapy play a part in every case. If the mentality of the patient is sufficiently high, reeducation of muscles may lead to improvement even after long periods of treatment. Violent

massage is often poorly tolerated and must be avoided. When the lesions are not extensive, antisyphilitic treatment combined with reeducation and the use of nerve sedatives and protective splints may suffice. Patients with long-standing conditions may be helped through the correction or prevention of deformity, the use of tendon transplants, the resection of sympathetic nerves or the Stoffel operation. It is as well to avoid too great enthusiasm or pessimism. If there is spontaneous progress toward improvement good results may be hoped for.

RYAN, Vancouver, Canada.

SEXUAL PSYCHOPATHOLOGIC REACTIONS IN INFANCY. G. MILIO, Arch. ital. di pediat. **2**:690 (Oct.) 1934.

This article is a didactic discourse on the etiology, classification and prevention of anomalous sexual development in childhood. Onanism, hyperesthesia, sadism, masochism, fetishism, exhibitionism and homosexuality are discussed in the light of their manifestations in early life. The author has drawn heavily on the works of von Krafft-Ebing and Moll without adding new material or interpretations of his own.

DOOLEY, New York.

THE NEUROVEGETATIVE SYSTEM: THE PROTECTIVE BARRIERS AND MENINGO-ENCEPHALIC REACTION IN INFANCY. GIOVANNI GENOESE, Pediatria **42**:1035 (Sept.) 1934.

This paper contains a complete review of the present knowledge of the physiopathologic features of the vegetative nervous system and the hemato-encephalic barrier and the author's analysis of the relations that exist between the vegetative nervous system, the barrier, the capillaries of the vascular system and the reticuloendothelial system. The author discusses several factors that may cause disturbances in the function of the barrier, and he maintains that certain therapeutic procedures are directly concerned with the production of meningo-encephalic reactions in infancy. He refers especially to the use of biologic and protein therapy, chemotherapy and physiotherapy.

The author directs attention to the fact that neurovegetative alterations may follow certain therapeutic impulses as well as marked modifications of the permeability of the capillaries with resulting alterations in the protective barrier. He illustrates that in certain instances, such as in those of predisposition, these phenomena may result in opening the way to invasion of the cerebral substance by the various ultraviruses and their toxins and to subsequent meningo-encephalic reactions.

SIGNORELLI, New Orleans.

LATENT SYMPTOMATOLOGIC AND BACTERIOCYTOLOGIC DISASSOCIATION IN PNEUMOCOCCIC MENINGITIS IN CHILDREN. ARGEO POUCHE, Pediatria **42**:1185 (Oct.) 1934.

Two cases of pneumococcic meningitis in infants are reported in which the clinical course was markedly atypical, owing to the absence of the usual physical findings, especially with reference to the reflexes.

The author calls attention to the disproportion between the mild clinical findings and the excessive pathologic changes observed at autopsy in each case; he also points out that in one case large numbers of micro-organisms (Pneumococcus) were exhibited with but slight tissue reaction.

SIGNORELLI, New Orleans.

EXPERIMENTAL RESEARCH ON THE RELATION OF POTASSIUM AND GUANIDINE: PATHOGENESIS OF SPASMOPHILIA. ALBERTO CABITTO, Pediatria **42**:1322 (Nov.) 1934.

The author cites the outstanding conceptions relating to the biologic activity and metabolism of potassium in cases of rickets and idiopathic tetany and in

experimental tetany induced by administration of guanidine. The author's investigations on the relation of potassium and guanidine in their action on the isolated heart of the frog showed that the potassium content of the medium influenced markedly the action of guanidine.

SIGNORELLI, New Orleans.

BLOOD CHOLESTEROL IN CASES OF EPILEPTIC CONVULSIONS IN CHILDREN AND OF SPASMOPHILIA. MARIA RAMPINI, Riv. di clin. pediat. **32**:1281 (Nov.) 1934.

For each of nine children with tetany and for twelve of twenty children with epilepsy, the level of cholesterol in the blood was found to be higher than normal. Immediately after a convulsion the amount of cholesterol in the blood definitely increased, and it remained higher than normal for several hours. On recovery from the spasmophilic state the level of the blood cholesterol declined to normal.

Hyperventilation in cases of epilepsy as well as in those of spasmophilia led to spasticity or convulsions; the cholesterol of the blood was increased to about the same level as in cases in which the convulsions were due to other causes.

The author does not believe that hypercholesteremia is a causative factor in convulsions.

HIGGINS, Boston.

PERMEABILITY OF THE MENINGES OF HEALTHY CHILDREN TO BROMIDES AND DIPHTHERIA ANTITOXIN. V. MENGOLI and V. MIGLIORI, Riv. di clin. pediat. **32**:1343 (Nov.) 1934.

In only one case in ten was the antitoxin in the spinal fluid found to exceed one-thousandth unit per cubic centimeter after from 2,000 to 80,000 units of diphtheria antitoxin had been given intramuscularly; in these cases from ½ to 6 units per cubic centimeter of blood was found. The permeability to antitoxin of the barrier between the blood and the spinal fluid is governed not wholly by physicochemical laws of diffusion but also by the secretory activity of the cells.

HIGGINS, Boston.

THE CONVULSIVE STATE IN INFANCY. EUGENIO CIENFUEGOS, Arch. de pediat., Rio de Janeiro **7**:49 (Nov.) 1934.

Convulsions should be classified as follows: those depending on a constitutional state, such as spasmophilia, laryngospasm, infantile eclampsia and tetany; those depending on lesions of the central nervous system; those with a symptomatic basis, such as initiation of a contagious disease, and those with an idiopathic basis, such as epilepsy. Each condition must be differentiated if the appropriate treatment is to be given.

SANFORD, Chicago.

POSTPNEUMONIC MENINGO-ENCEPHALITIS. WALTER PIAGGIO GARZÓN, Med. de los niños **35**:261 (Sept.) 1934.

In a girl, aged 2½ years, muscular rigidity with tonic and clonic spasms developed after the crisis in pneumonia. The spinal fluid showed an increased amount of albumin and lymphocytosis but no organisms. Paralysis of the respiratory muscles appeared early, and after two weeks the child died in coma.

H. L. DWYER, Kansas City, Mo.

CEREBRAL DISTURBANCES IN CHILDHOOD AND THEIR ENCEPHALOGRAPHIC DIAGNOSIS: I. THE PERFORMANCE OF ENCEPHALOGRAPHY. KARL RUPILIUS, Arch. f. Kinderh. **103**:32, 1934.

The use of encephalography in the study of cerebral disorders in children is discussed under these headings: anatomy of the cerebrospinal spaces, preparation of the patient, technic of the introduction of air, technic of the roentgen examination, indications for encephalography and the normal encephalogram.

LEMASTER, Evanston, Ill.

CEREBRAL DISTURBANCES IN CHILDHOOD AND THEIR ENCEPHALOGRAPHIC DIAGNOSIS: II. THE PATHOLOGIC ENCEPHALOGRAM. KARL RUPILIUS, Arch. f. Kinderh. **103**:156, 1934.

The appearance of the encephalogram in the following conditions is described: acute encephalitis, cerebral paralysis, feeblemindedness without paralysis, hydrocephalus, microcephalus, deafness, congenital syphilis, tumors of the brain, true epilepsy, mongolian idiocy, poliomyelitis and meningitis.

LEMASTER, Evanston, Ill.

A CASE OF FRIEDREICH'S ATAXIA. PAUL VON KISS and ISTVÁN FÉNYES, Arch. f. Kinderh. **103**:237, 1934.

A case of Friedreich's ataxia in a 14 year old boy is reported. No history of familial occurrence could be elicited. Symptoms began when the child was 4 years old.

LEMASTER, Evanston, Ill.

CISTERNAL AND LUMBAR DRAINAGE IN THE TREATMENT OF COMA FROM ACUTE BARBITAL POISONING TOGETHER WITH OBSERVATIONS ON CHRONIC BARBITAL POISONING. JAMES PURVES-STEWART, Jahrb. f. Psychiat. u. Neurol. **51**:203, 1934.

Purves-Stewart points out that barbital derivatives are more powerful and potentially more dangerous than barbital itself, while the confusing claims for the various barbituric compounds, which are so assiduously placed on the market, induce a physician who has perhaps found barbital unsatisfactory to turn to one or other of the barbital derivatives until he learns, by bitter experience, that it is only a similar drug under a new name. When barbital or one of its modifications is taken continuously for prolonged periods, even in ordinary therapeutic doses of from 32 to 65 cg., careful supervision is always necessary because the effects on the central nervous system do not always limit themselves to the desired hypnotic effect. Sometimes a cumulative and localized pathologic reaction may appear in other parts of the nervous system, such as the mesencephalon, the cerebellum and even the spinal cord, producing syndromes for which the patient may come under the care of the neurologist. In some cases the repeated use of such drugs may lead to drug addiction. Moreover, the barbital group of drugs has in recent years become increasingly popular as serving suicidal purposes.

To illustrate the toxic effect of moderate therapeutic doses of these drugs on the nervous system, Purves-Stewart describes in detail a case of poisoning due to barbital sodium in which the symptoms were referred to the posterolateral portion of the spinal cord, a case of poisoning due to a barbital derivative with aminopyrine in which a cerebellar syndrome resulted and a case of poisoning due to barbital sodium, a midbrain syndrome being produced.

In discussing acute barbital poisoning Purves-Stewart recalls that the physiologic effects of barbital and its allies include not only a specific hypnotic effect on the brain, for which they are ordinarily prescribed, but also an effect on the heart, lungs and kidneys. Larger doses, or in susceptible patients ordinary doses, cause acute and sometimes fatal coma. The most common symptoms of acute barbital poisoning are profound coma, with moderately contracted pupils, usually reacting to light, flaccidity of the limbs and loss of tendon reflexes, extensor plantar responses and abdominal reflexes. The heart rate is rapid; cyanosis sets in, and the blood pressure drops owing to the toxic effect on the myocardium. Blisters may appear on the skin, especially at sites of pressure. The drug is excreted rapidly into the urine and cerebrospinal fluid. In some cases suppression of urine may occur. There is generally terminal bronchopneumonia with pyrexia, and death occurs from cardiac failure.

The average minimum fatal dose is about 3.25 Gm., although 1 Gm. has been known to prove fatal. On the other hand, recovery has occurred under suitable

treatment with doses as large as 13 Gm., and the author has observed a case of recovery after a single dose of 31 Gm. of barbituric compounds.

Treatment for acute barbital poisoning, as commonly carried out, includes prompt gastric lavage with warm water to remove any of the drug which may still remain in the stomach. About 550 cc. of hot coffee mixed with 120 cc. of a 10 per cent solution of dextrose and 30 cc. of castor oil is left in the stomach. The gastric lavage is repeated every four to six hours, two or three times. Colonic irrigation is also resorted to at once and is repeated two or three times at intervals of twelve hours, followed by the rectal administration of dextrose. Warmth is applied to the body, and cardiac stimulants are given hypodermically every two hours, while strychnine hydrochloride in maximal doses (4 mg. at a time) and picrotoxin (2.5 mg.) are also given intensively. Inhalations of oxygen and carbon dioxide by nasal tube are helpful. The urine is withdrawn by catheter and, like the contents of the stomach, is preserved for chemical analysis.

These are the ordinary measures employed in cases of acute barbital poisoning. The most urgent indication, after washing out of the stomach, is to accelerate the removal of the drug from the nervous system and especially from the medullary centers which are continually bathed by the poison in high concentration. If, therefore, cerebrospinal fluid is withdrawn by lumbar puncture or better still by cisternal puncture and if meanwhile no fresh barbital is being absorbed into the circulation, the new cerebrospinal fluid excreted by the choroid plexus will contain progressively diminishing quantities of the drug, and the prospects of recovery will be materially improved. The paper concludes with a detailed report of five cases of attempted suicide by means of unusually large doses of a barbital compound; in all the cases the foregoing method of treatment was used with complete recovery.

KESCHNER, New York. [ARCH. NEUROL. & PSYCHIAT.]

RESULTS OF ENCEPHALOGRAPHY IN EPILEPSY. A. WAND, Med. Klin. **31**:48 (Jan. 11) 1935.

Of thirty patients with epilepsy who were studied by means of encephalography, three had tumor of the brain and three dilatation and distortion of the ventricles. In more than half of the remaining patients there was significant diminution in the number of convulsions after the injection of air. The author believes that in every case of epilepsy at least one encephalogram should be made as a diagnostic if not as a therapeutic procedure and that certain patients may be improved by receiving repeated injections of air.

DOOLEY, New York.

ACUTE OPTIC NEURITIS WITH SUDDEN, TRANSIENT BLINDNESS AS A PRIMARY SYMPTOM OF ACUTE ANTERIOR POLIOMYELITIS: REPORT OF A CASE. V. MUCH and A. HÜPPI, Klin. Monatsbl. f. Augenh. **93**:333 (Sept.) 1934.

A case of acute anterior poliomyelitis in a woman, aged 37, is reported in detail, and the report is illustrated with eight charts of the fields of vision. The peculiar symptoms are discussed. The first symptoms were headache and a "cold," which were followed by reduction of vision to mere perception of light on the third day. The ocular symptoms were severe acute optic neuritis, disturbances of the pupils (paralysis of the sphincter and anisocoria) and paralysis of the muscles of accommodation. Sensory disorders did not exist during the course of the disease, and the meninges were only slightly involved. The authors exclude a connection between the inflammation of the optic nerve and that of the spinal cord. In their opinion an infectious virus was present and gave rise to the optic neuritis. This initial symptom was followed by the inflammation of the spinal cord. The optic neuritis was a localized process, not caused via brain centers or meninges. The disturbances of accommodation and the internal ophthalmoparalysis were caused by a lesion of the nuclear area by the virus analogous to the process in the optic nerve. The authors are inclined to interpret the lack of correlation between the reaction to light and that in accommodation as the Argyll Robertson phenomenon.

Inhalation of amyl nitrite seems to have been at least contributory in completely restoring the function of the optic nerve, as it had been in previous cases observed by the authors.

STOLL, Cincinnati. [ARCH. OPHTH.]

SIGNIFICANCE OF OVEREXTENSION OF MUSCLES IN PARALYSIS. P. VON PUKY, München. med. Wchnschr. **81**:1505 (Sept. 28) 1934.

Extensive paralysis may disappear after the acute stage of poliomyelitis. Almost always some paralyzed muscles recover. The period of reparation is from one to two years. During this period recovery is possible for the muscles for which the spinal nerve cells have not been destroyed but which have only temporarily lost their function as a result of inflammatory edema during the acute stage. Whether paralysis of a muscle is due to the destruction or the loss of function of its nerve cells can be determined only by the duration of the paralysis. Galvanization is not the proper treatment for the paralyzed muscles. The author stresses the importance of massage and exercise while the muscles are relaxed and protected against overextension. Overextension may permanently damage them. In the cases in which proper treatment is not given, operative removal of contractures may be necessary.

BRAHDY, Mount Vernon, N. Y.

PHOSPHATIDE CONTENT OF THE BRAIN IN NIEMANN-PICK'S DISEASE AND IN INFANTILE AMAUROTIC IDIOCY. E. EPSTEIN, Virchows Arch. f. path. Anat. **293**:135, 1934.

Cases in which enlargement of the spleen and the hepatic changes of Niemann-Pick's disease are associated with the retinal changes of Tay-Sachs' disease have led to controversy as to whether they are examples of a combination of the two diseases and whether phosphatide lipoidosis and infantile amaurotic idiocy are two distinct diseases or two types or stages of the same disease. Epstein's previous chemical work, which has been confirmed by others, showed that the characteristic feature of Niemann-Pick's disease is the storage of phosphatide lipoids in the reticulo-endothelial system. The brain contained twice as much phosphorus in the form of ether-soluble and alcohol-soluble lipoids as the brain of a normal child. Epstein now reports the results of his chemical investigation of three brains from children with amaurotic idiocy. The brains were fixed in a solution of formaldehyde. As a control, the similarly fixed brain of a normal child of the same age was examined. The amount of lipoid phosphorus was not increased but was definitely decreased as compared with those of the normal brain. Epstein concludes that the two diseases in question are distinct and that the retinal lesion of phosphatide lipoidosis is not the same as that of amaurotic idiocy. In a second part of the paper Epstein and Lorenz discuss the changes that occur in the phosphatides when the brain is preserved in a solution of formaldehyde. A progressive decrease in the amount of phosphatides occurs, owing to their gradual transformation into water-soluble compounds. A true estimate of the phosphatide lipoids is not possible unless the brain has been kept in the original solution of formaldehyde, which must also be chemically examined. They believe, furthermore, that the chemical changes described affect the conclusions to be drawn from microchemical stains for lipoids if the material has been long in a solution of formaldehyde.

SCHULTZ, Evanston, Ill.

REPORT OF A CASE OF MENINGITIS DUE TO PROLONGED EXPOSURE TO DIRECT RAYS OF THE SUN. JAN ZIENKIEWICZ, Pedjatrja polska **14**:82, 1934.

According to the results of the author's investigation, meningitis due to exposure to the rays of the sun is rare. He found only three cases reported in the literature. The patient whom he observed had acute meningeal symptoms, which, however, were quickly relieved by frequent spinal punctures. Decompression was contemplated in case the patient did not improve.

KRUPINSKI, Chicago.

EVOLUTION OF INTELLIGENCE OF INFANTS BORN IN THE SPRING AND OF THOSE BORN IN THE AUTUMN. C. LOOFT, Acta pædiat. **15**:381 (Sept. 5) 1934.

In 1929 Blonsky studied a small group of children in Moscow with reference to a possible correlation between the season during which they were born and their subsequent development. He arrived at the conclusion that infants born in the spring show better physical progress and evidence a higher intelligence quotient when examined later in childhood than those born in the autumn. Cchiøtz and Seland conducted an inquiry into the same problem on a much larger group of children in Oslo, Norway, and the method employed in their study was more reliable. They found no demonstrable difference in the subsequent physical development of children born in the two seasons.

The present contribution is a statistical investigation into the mental development of a large group of children in Bergen, Norway; 368 children were born between April and October and 343 between October and April. No correlation was discovered between the season of birth and the subsequent evolution of intelligence. Although fair weather during the first six months of life is conducive to satisfactory physical progress, climatic conditions during the second semester of the first year are also of great importance in this respect and possibly, in a secondary sense, in the unfolding of intellect. It is conceivable that rickets, tetany and other diseases the occurrence of which is conditioned by seasonal influences may affect a brain of inferior origin. Prenatal and postnatal factors have an importance equal to that of the season of birth. Poor heredity is the commonest cause of moderate mental retardation.

McCUNE, New York.

SPONTANEOUS PERFORATION OF A HYDROCEPHALUS THROUGH THE LARGE FONTANEL. H. DE JAGER, Nederl. tijdschr. v. geneesk. **78**:3954 (Sept. 1) 1934.

In a child with hydrocephalus associated with hydrorachis lumbosacralis, spontaneous perforation occurred through the large fontanel eight months after birth. After nearly all the spinal fluid had drained off, death occurred in two and a half days.

VAN CREVELD, Amsterdam, Netherlands.

ANATOMICOCLINICAL STUDY OF THE PALLIDAL SYNDROME IN CHILDHOOD. L. DE VOS and L. VAN BOGAERT, Nederl. tijdschr. v. geneesk. **78**:4073 (Sept. 8) 1934.

In a mentally deficient boy suffering from bilateral athetosis which had not progressed for five years, a peculiar form of motor excitability abruptly developed at the age of about 10 with such intensity that death occurred, chiefly owing to the inability to take food. On histopathologic examination symmetrical degeneration in both nuclear segments of the pallidum was observed. Traces of inflammation were noted in other regions, especially in the optic nerves and the walls of the ventricles. The following reconstruction of the pathogenesis may be made: encephalitis (certainly not of the epidemic type) with elective localization of the toxins in the pallidum and degeneration of the nuclei in this region, the atrophic process becoming stationary with persistence of the athetosis. The acute hyperkinesia and fatal evolution in the last weeks of life cannot be explained on the basis of results of the histologic examination. Observations similar to those in this case have rarely been recorded in the literature and then usually incompletely.

VAN CREVELD, Amsterdam, Netherlands.

MICROCEPHALIA VERA. R. BRUMMELKAMP, Nederl. tijdschr. v. geneesk. **78**:4286 (Sept. 22) 1934.

On the basis of six cases of microcephalia vera, in one of which observation was made by the author and five of which were cited from the literature, it is demonstrated that in respect to this condition Dubois' cephalization theory is valid.

VAN CREVELD, Amsterdam, Netherlands.

REMARKABLE DISTURBANCES OF LABYRINTHINE AND OPTIC REACTIONS IN A CASE OF HYDROCEPHALUS INTERNUS. G. G. J. RADEMAKER, Nederl. tijdschr. v. geneesk. **78**:4815 (Oct. 20) 1934.

The author describes a case of hydrocephalus internus in a girl aged 8 months, who was unable to keep the head upright. Disturbed function of the labyrinths must be accepted as the cause of this phenomenon, since other labyrinthine reactions could not be elicited. Absence of rotatory nystagmus and the presence of horizontal and vertical nystagmus point to involvement of the central portion of the vestibular system (Aubrey). Examination of the optic reactions revealed that subcortical but not cerebral optokinetic nystagmus could be elicited. In man, as in animals, subcortical optokinetic nystagmus exists.

VAN CREVELD, Amsterdam, Netherlands.

CONGENITAL DISTURBANCE OF FUNCTION OF THE MOTOR CRANIAL NERVES. R. VEDDER, Nederl. tijdschr. v. geneesk. **78**:5366 (Nov. 24) 1934.

The author describes three cases of congenital disturbance of function of the motor cranial nerves, the first in a boy of 10 years and the second and third in a brother and sister aged 12 and 17 years, respectively. He points to the familial character of the disease in these two children; thus, it becomes highly probable that the disturbance is the consequence of a defect in development.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ear, Nose and Throat

MORTALITY IN OTOGENIC INTRACRANIAL DISEASE. M. TAMARI, Monatschr. f. Ohrenh. **68**:1190 (Oct.); 1310 (Nov.) 1934.

Tamari's studies are based on observations made at necropsy at the general hospital in Vienna from 1895 to 1929, inclusive. This period followed that which was analyzed by Gruber; that is, it began at a time when otologic surgery was at the threshold of its modern development and when otogenic complications and pathologic conditions of the labyrinth were being commonly recognized. In comparing his tables with those of Gruber the author finds that the number of deaths due to disease of the ear not only has not decreased, but has become more than doubled in thirty-five years. In the reports of 40,000 necropsies analyzed by Gruber the deaths from aural disease amounted to 0.58 per cent; in the author's 82,000 necropsies they amounted to 1.29 per cent. In analyzing this enormous increase the author finds that it is especially great among children. Moreover, in the earlier statistics there frequently appear remarks about cryptogenic meningitis, and nothing is to be found about labyrinthogenic meningitis, while in the author's material the latter was mentioned seventy-six times. He thinks that this is due to the relatively late recognition of labyrinthogenic complications. The question as to whether the increased mortality rate of otogenic intracranial complications is the result of the greater surgical activity, he answers in the negative. He points out that almost until the end of the last century, sinus thrombosis as well as meningitis were considered to be incurable disorders and no surgical treatment was given. On the other hand, it appears that as a result of surgical prophylaxis and technical improvements in labyrinthine operations, a greater number of patients with otogenic complications are being saved. To prove this the author cites statistics reported by Neumann, whose figures demonstrate conclusively the success of surgical intervention in the presence of an otogenic complication. The author is inclined to agree with Heymann, who believes that the mortality in cases of otogenic complications is really not greater than formerly but that the development of otiatrics has made the danger involved in suppurative otitis media the general knowledge of physicians, and thus a greater number of cases are being recognized.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

NATURE OF STUTTERING. A. VON SARBÓ, Monatschr. f. Ohrenh. **68**:1374 (Nov.) 1934.

Von Sarbó explains the development of stuttering on an emotional basis. He shows that the interbrain and midbrain in connection with the extrapyramidal tracts explain the symptoms of stuttering completely. In the last analysis, speaking is an expression of the existing state of mind. The psychic components enter later, but, acting by way of the emotional status, they may make it difficult for the organs of speech to function smoothly. The structural conditions of the region, which harbors also the highest vasomotor center, determines whether or not a person is predisposed to stuttering. The author believes that further research will bring anatomic proof of a predisposition to stuttering.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

CLINICAL AND PATHOLOGIC ASPECTS OF CHRONIC TONSILLITIS AND OF CHRONIC IRRITATION OF TONSILLAR CRYPTS. E. E. ERTL, Monatschr. f. Ohrenh. **68**:1419 (Dec.) 1934.

Ertl shows that the changes which Dietrich designated as characteristic of chronic tonsillitis are found also in patients whose anamnesis reveals no history of tonsillar disturbances and who have no clinical symptoms that are indicative of tonsillar disease, with the exception of detritus (intermingled with leukocytes) in the lacunae. In spite of the fact that the pathologic process in chronic tonsillitis is usually more severe, it is not always possible to differentiate between these two disturbances on the basis of the number and the extension of the pathologic processes. An increase in the number of leukocytes in the lacunar streak demonstrates that pathologic processes can be present in the crypts and not disclosed by the anamnesis. Thus it is understandable how careful clinical examination discloses the fact that 71 per cent of the patients who have no history of tonsillar disturbances and whose tonsils are free from signs of inflammation have an increased number of leukocytes in the tonsillar lacunae. The inflammation that develops in the lacunae is caused by the retention of cell rests and later of bacteria and fungi in the crypts. This retention is due to the fact that the cleansing of the crypts is more difficult because of the presence of scar tissue, postinflammatory adhesions, cavities and pockets and because of the constriction of the lacunae resulting from hypertrophy of the tonsils. The ratio of lymphocytes to leukocytes found in the streak does not warrant the drawing of conclusions as to the presence elsewhere of rheumatism, for instance, for the ratio fluctuates not only in different patients who have the same symptoms but also in the same patient at different times.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

RELATIONSHIP BETWEEN STUTTERING AND PARAPHRASIA (TACHYLALIC). H. FREUND, Monatschr. f. Ohrenh. **68**:1446 (Dec.) 1934.

After citing reports from the earlier literature in which it was maintained that the overhasty speech movements in cases of paraphrasia may develop into stuttering, Freund shows that the same underlying causes may give rise to paraphrasic disorders of speech or to stuttering. He further shows that in spite of the close relationship between the two disorders there also exist certain contradictions, which he lists in opposite columns of a table. He also cites and analyzes a number of case reports. In summarizing his observations on the relationship between stuttering and paraphrasia he states that there is a paraphrasic form of stuttering which has all the aspects of paraphrasia and in which the diagnostic and the therapeutic differentiation are of no significance. Almost the same can be said about "initial" and "rudimentary" stuttering. In spite of characteristic symptoms of stuttering, such as phonophobia, logophobia, a feeling of phonetic incompetence, fear of difficult words and internal stuttering, the basis of the tachylalic paraphrasia is essentially paraphrasic. Stuttering is a superimposed disorder which develops

inductively from the conditions that obtain in tachylalic paraphrasia, and stuttering disappears with the appearance of tachylalic paraphrasia. The paraphrasic foundation facilitates therapeutic modification. The logopedic therapy of this form of stuttering is identical with that which is employed in tachylalic paraphrasia and counteracts the symptoms of stuttering. The author gained the impression that the disorder is especially frequent during puberty. In persons with a number of nervous and neurotic symptoms the disorder is especially likely to develop.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

OTITIDES OF INFANTS AND THE RELATION BETWEEN OTITIDES AND INTOXICATION. M. LITSCHKUS, München. med. Wchnschr. **81**:1492 (Sept. 28) 1934.

Otitis occurs frequently in infants and is often not diagnosed. In every obscure febrile disturbance the ears should be carefully examined. Likewise, in intestinal disturbances which are not due to faulty nutrition, otoscopy is essential. One must recognize that there is a relation between intestinal intoxication of nonalimentary character and purulent otitis media, and in the majority of cases the otitis is the primary disorder. It is desirable for every pediatrician to master the technic of otoscopy. (The article comes from Russia.) BRAHDY, Mount Vernon, N. Y.

LATE STUTTERING AND LATE STUTTERERS. J. SUSMANN, München. med. Wchnschr. **81**:1578 (Oct. 12) 1934.

Susmann reports some observations in six hundred and four stutterers from 2 to 26 years of age. The highest incidence of the onset was in the fifth year of life, when it was 18.5 per cent. In each succeeding year until the end of the eighth year the incidence remained high, namely, 9.6 per cent. The speech apparatus in early childhood is a locus minoris resistentiae, phylogenetically new, and under certain traumas (physical or psychic) may show evidence of functional incoordination. The stuttering which occurs after puberty is in most cases a symptom of a traumatic neurosis. Fright is the etiologic factor in children in from 68 to 80 per cent of the cases, whereas in adults it is the etiologic factor in only 9.1 per cent. Stuttering starting after puberty is less amenable to treatment.

BRAHDY, Mount Vernon, N. Y.

Surgery and Orthopedics

TALIPES EQUINO-VARUS. DENIS BROWNE, Lancet **2**:969 (Nov. 3) 1934.

This article is an attack on the whole of present teaching about this condition. The attack turns on three main points:

1. The acceptance of the compression hypothesis of the causation of talipes places it in a definite group of congenital deformities, explains all its variations of structure and function and gives a valuable clue to its treatment by showing the true nature of the deformity. 2. The essential physiologic principle in treatment is that structure and function shall be corrected simultaneously, in other words, that the foot must be kept active while its shape is being corrected. 3. The essential mechanical principle is that the position of one foot can be controlled by the other in relation to the sagittal plane of the body.

In infants (up to 2 years of age) correction of the longitudinal arch is accomplished by the hands alone. When the feet are too stiff a wooden arrangement resembling a large pair of nutcrackers is used. LANGMANN, New York.

FLAT-FEET. PHILIP WILES, Lancet **2**:1089 (Nov. 17) 1934.

A flat foot, accurately speaking, is one which is structurally built so as to have a low arch when the foot is in the ideal posture for that person. This type of foot is not uncommon; it is not pathologic and must be carefully dis-

tinguished from the pathologic condition of an everted, abducted foot which is usually called flatfoot but should more appropriately be termed pes valgus. The plump infant, who is likely to grow into the sthenic type, has an obvious longitudinal arch and maintains this arch when he starts to walk. The asthenic infant, on the other hand, with long thin feet, is frequently found to have extremely valgus feet as soon as he begins to stand. The majority of the latter group improve spontaneously at about from 4 to 6 years of age. A short tendo Achillis is a fairly common factor in the production of valgus feet; poliomyelitis is another cause. Then there are those cases in which the pes valgus is part of the faulty posture of the whole body and finally those in which the faulty posture of the foot is due to muscular failure or congenital maladjustment.

Muscular education or reeducation is the method employed in the last group. The most that arch-supports can do is to give some help to a patient who can produce a voluntary correction. As a general rule, at any rate in the treatment of children and younger adults, they should be avoided. The object is to teach the muscles to maintain a new posture, and any mechanical aid is likely to interfere with the acquisition of the new muscle balance. LANGMANN, New York.

THE DIAGNOSIS AND TREATMENT OF EMPYEMA. L. S. T. BURRELL, Practitioner **134**:7 (Jan.) 1935.

Burrell discusses empyema, dividing it into two classes: nontuberculous and tuberculous. He points out that the patient with the first type is febrile and has the usual signs and symptoms associated with sepsis; the patient with the second type may remain free from symptoms for a long period.

The nontuberculous type may be due to such causes as a ruptured abscess, carcinoma, suppuration from below the diaphragm or injury, but in the majority of cases the condition follows either pneumococcic or streptococcic pneumonia. In regard to the diagnosis, stress is given to the statement that a definite diagnosis of empyema should never be made without aspiration.

The technic of puncture is discussed in detail.

Burrell states that the chief objective of the treatment is removal of the fluid, but he warns against the possible danger of producing an open pyothorax. In this regard he points out that during the influenza epidemic in 1918 it was found that a mortality of more than 50 per cent following early operation and drainage was reduced to below 10 per cent by delaying operation until adhesions had formed. While the fluid is thin aspiration is indicated, but after frank pus has developed treatment by intercostal drainage or resection of ribs is in order.

The four principles of treatment suggested in cases of nontuberculous empyema are: (1) to evacuate the pus; (2) to sterilize the pleural cavity; (3) to obtain reexpansion of the lung; (4) to improve the general condition of the patient. The first principle has already been noted. Under the second, Burrell suggests using gentle irrigations of the cavity every two hours during the day until reexpansion of the lung has occurred. Surgical solution of chlorinated soda or an acid solution of sodium hypochlorite (eusol) is recommended. Simple medication, diet and general care are also discussed.

Tuberculous empyema occasionally develops in the course of pulmonary tuberculosis. It may also occur as a complication of artificial pneumothorax. It usually starts as a clear tuberculous effusion, in which event the liquid first becomes cloudy, gradually becomes thicker and finally is the typical greenish tuberculous pus. Patients with chronic tuberculous empyema may remain in good health and keep at work for years; however, the infection generally proves fatal in the end. If left alone the empyema may rupture into the lung, and, on the other hand, if repeated aspirations are made a sinus may develop. When a large empyema cavity is present with a completely or almost completely collapsed lung, aspiration of the pus and irrigation of the cavity are indicated, and an attempt should be

made to reexpand the collapsed lung. If this fails to bring about reexpansion, the author advises thoracoplasty. Detailed instructions for the aspiration of fluid are given.

SAPPINGTON, San Francisco.

CHRONIC INTUSSUSCEPTION. F. C. PYBUS, Proc. Roy. Soc. Med. **27**:1325 (Aug.) 1934.

A boy, aged 7 years, was admitted to the hospital with the history that he had had an attack of abdominal pain, vomiting and diarrhea seven weeks previously and that since there had been progressive loss of weight. On examination the abdomen was full; the left flank was dull on percussion, and a mass was found in the upper part of the abdomen. A diagnosis of tuberculous peritonitis was made. A week later the boy had another attack of pain and vomiting and passed blood per rectum. Two months later another severe attack occurred, and then a diagnosis of chronic intestinal obstruction was made. A few weeks later he was seen by the surgeon, who made a diagnosis of chronic intussusception of six months' duration. At operation the intussusception was found to be of the ileocecal type.

WILLIAMSON, New Orleans.

THE AFTER-EFFECTS OF HEAD INJURY. W. RITCHIE RUSSELL, Tr. Med.-Chir. Soc. Edinburgh, 1934, p. 129; in Edinburgh M. J., Sept. 1934.

Two hundred patients reported back after the acute stage. The author analyzes their progress. Postconcussional symptoms were present in 60 per cent of the total number of cases. Children under 10 years and adults over 40 years of age had the highest percentage of such later symptoms, those over 50 all showing these manifestations. The after-effects in the 120 cases lasted from two to six months in 9 per cent, from six to eighteen months in 25 per cent and more than eighteen months in 66 per cent. The patients are primarily kept in the hospital for three weeks as a routine practice.

One boy, aged 7 years, with a fissure fracture of the right parietal region, was unconscious for twenty-four hours. He became irritable and difficult to control eighteen months after the accident.

Aphasia and severe mental enfeeblement may come after gross injuries. Young adults show remarkable ability to recover and do full work at their employment.

NEFF, Kansas City, Mo.

COXA VARA AT ADOLESCENCE FOLLOWED THROUGHOUT ITS COURSE. A. TRÈVES, Bull. et mém. Soc. d. chirurgiens de Paris **26**:442 (July 6) 1934.

Trèves exposed the lesion and followed the case with roentgenograms. Eighteen months earlier the boy had presented a circular incurving of the limbs which required forcible straightening. From his fourth year he had been obese. At the age of 5 years he was operated on for inguinal hernia. At the beginning of October 1933 he began to limp with his left leg, but had no pain. In a roentgenogram taken on October 6 there was seen a slight enlargement, indistinctly outlined, of the diaphyseal cartilage of the left femur on the outer side. Motion of the hip joint was almost normal, but there was a slight limitation of abduction and internal rotation. On October 28 the condition had become worse. The claudication had increased, and walking was difficult and painful. A roentgenogram showed a considerable increase in the epiphysiolysis. There was a complete epiphyseal detachment of the femoral head, with outward displacement of the neck. The interarticular line was normal. On Nov. 4, 1934, the boy was allowed to be up, and he gradually resumed walking. Thyroid treatment had been given for his obesity, and he had lost 17 pounds (7.7 Kg.). A roentgenogram taken on June 20 showed healing to be complete. This condition was plainly coxa vara of endocrine production.

VINTON, Brooklyn.

Miscellaneous

AGE CHANGES IN PHYSICAL RESEMBLANCE OF SIBLINGS. CARROL E. PALMER, Child Development **5**:351 (Dec.) 1934.

The data for this study were collected by the Office of Child Hygiene, United States Public Health Service, of Hagerstown, Md., during an extensive seven year investigation of the physical growth of more than 2,500 white school children in the elementary grades. One hundred and ninety-three pairs of brothers and 154 pairs of sisters were observed during the age period of from 7 to 12. The physical measurements of height and weight of the siblings at successive ages showed that the coefficients of correlation for height and weight of brothers and sisters decreased as the age increased from 7 to 12. Fraternal resemblance in physical characteristics was less marked at 12 than earlier and "less than it will be later, say in early adult life." The data also indicated that boys who have brothers and girls who have sisters tend to be lighter in weight and slightly shorter, on the average, than a large group of boys and girls in the general population. Siblings also tend to be less variable in weight than the general group of boys and girls.

ABRAMSON, New York.

JUVENILE DELINQUENCY A PRODUCT OF THE HOME. T. EARL SULLENGER, J. Crim. Law & Criminol. **24**:1088, 1934.

The family is the prime determiner of social behavior. From it comes youth indelibly stamped with noble aspirations or with low, vile antisocial attitudes toward life. The family today is less stable than it has been at any time since the beginning of the Christian era. Out of this situation comes much juvenile delinquency. Burt's study in London showed that 60 per cent of the delinquents studied came from broken homes. The results of a study of two groups of delinquents in Omaha are summarized in the tables. One table shows that in one group 50.7 per cent of the delinquents were from broken homes; the other table is presented to show the percentage of delinquents from the various types of broken homes. This leads to the inevitable conclusion that the broken home all too frequently is a breeding place for the criminals of tomorrow; it behooves society to remedy this condition and thus remove one of the chief groups of determinants of juvenile delinquency.

SELLING, Chicago [ARCH NEUROL. & PSYCHIAT.]

STUDIES ON BARBITURATES: IX. THE EFFECT OF BARBITURATES ON THE EMBRYO AND ON PREGNANCY. JAMES M. DILLE, J. Pharmacol. & Exper.Therap. **52**: 129 (Oct.) 1934.

The author shows that barbiturates (amytal and barbital) readily penetrate the placenta of laboratory animals, attaining at times anesthetic levels in the embryo. He therefore urges caution in the "use of these drugs in pregnant women."

PILCHER, Cleveland.

ATROPINE TOLERANCE IN INFANTS AND CHILDREN: NEGATIVE ACTION OF THE SERUM OF TOLERANT SUBJECTS. J. D. PILCHER, J. Pharmacol. & Exper. Therap. **52**:196 (Oct.) 1934.

The blood serum of rabbits with a tolerance for atropine neutralizes the action of large quantities of atropine. The serum of infants having a tolerance for atropine had no such action. Large doses of atropine or its constituents (levorotatory and dextrorotatory hyoscyamine) produced deep sleep in tolerant subjects without excitation. (The narcotic effect of atropine has been observed in normal subjects by other investigators.)

PILCHER, Cleveland.

ETHYL ALCOHOL AND STRYCHNINE ANTAGONISM. H. GOLD and J. TRAVELL. J. Pharmacol. & Exper. Therap. **52**:345 (Nov.) 1934.

Alcohol proved to be an effective antidote in animals (the cat, dog and rabbit) against several times the fatal dose of strychnine. The authors state: "The most effective protection is obtained by the use of large doses of alcohol administered orally, followed by small doses given intravenously throughout the course of the poisoning whenever excessive hyperexcitability or convulsions occur." Caution is advised, as alcohol administered intravenously by this method readily paralyzes respiration. Judiciously used, ether proved to be even more efficacious in strychnine poisoning (in the cat). Great caution must be used with very large doses of strychnine lest strychnine and ether act synergistically in depressing respiration. Etherization to the point of abolition of hyperexcitability is the desired end. No doubt, artificial respiration also would be an effective aid.

PILCHER, Cleveland.

DISTRICT HEALTH PROGRAM IN RURAL AREAS. IRL B. KRAUSE and WILLIAM F. LUNSFORD, South. M. J. **27**:869 (Oct.) 1934.

The advantages of district organization in rural areas are as follows:

1. The opportunity for the selection of a trained personnel without local interference.

2. Improved security of tenure of office for the district director, he being a field supervisor for the state department of health.

3. Improvement in cooperation between the district health officer and the practitioner, due to the fact that the district director, by the nature of his position, would not be considered a competitor in the field of medicine.

4. Impartial management of the public health work in counties comprising the district.

5. Ability to employ graduate sanitary engineers instead of sanitary inspectors. It is understood, of course, that inspectors would be needed temporarily for individual home sanitation.

6. Availability of nurses for assignment to other localities in an emergency, although they would work in individual counties comprising the district.

7. Economy of operation, which is one of the most salient reasons for institution of this scheme in sparsely settled areas.

8. An opportunity to develop public health education unselfishly, which, after all, means development of a local health consciousness, which would lend to individual and community cooperation, demanding adequate appropriation for advancement of public health.

9. Avoidance of duplication of effort, which is often seen in county public health work.

SCHLUTZ, Chicago.

TWENTY YEARS OF COUNTY HEALTH WORK IN NORTH CAROLINA. JOHN H. HAMILTON and D. F. MILAM, South. M. J. **27**:875 (Oct.) 1934.

The authors conclude that a county board of health should be composed of members whose principal official allegiance is to the health program of the county.

County departments of health should be unhampered by demands for the treatment of sick indigent persons.

The state should subsidize county health work. The method of allocating the subsidy should encourage the adoption of a balanced program.

The state should offer to the local health program a consulting and coordinating service.

Forms for reports of activity and financial statements should be adapted to conform to the size of the local unit.

A balanced program, which can be provided only by a qualified health officer, a trained public health nurse, an efficient clerk, a competent sanitary inspector and a dentist informed in oral hygiene, should be required of every local department of health that is to receive aid from the state. If the county is unable to pay its share of the cost of this type of service for an entire year, it should at least have a part of the service which can be rendered by this organization.

SCHLUTZ, Chicago.

THE FOUNDATION OF LONGEVITY. HUGH LESLIE MOORE, South. M. J. **27**:983 (Dec.) 1934.

The author believes that the first step in laying the foundation of longevity is the transmission of good health as well as good character to one's offspring. He recommends promotion of legislation providing for vasectomy of all habitual criminals. Mentally defective persons should be sterilized.

Antepartum care as well as the best obstetric care should be provided for every expectant mother. The greatest opportunity for prevention lies in the field of pediatrics. The author believes that children of the better classes under the age of 2 years receive adequate medical care. The same is true of this group after they reach school age. It is the child between the ages of 2 and 6, who can run about, who is neglected. This is not only true of the child in the average family but equally so of that of the well-to-do. During this preschool age, preventive measures are forgotten; and medical advice is seldom sought or proffered, except when the child is acutely ill.

The greatest single factor in preventive medicine is proper nutrition. The present knowledge of preventive medicine and hygiene is not adequately used.

SCHLUTZ, Chicago.

HOW MAY THE HEALTH OFFICER DETERMINE AN EFFECTIVE PRENATAL SERVICE? M. H. JENSEN, South. M. J. **27**:1047 (Dec.) 1934.

This nation still leads the civilized world in allowing mothers to die in childbirth.

At least 165,000 fetal, neonatal and maternal deaths occur each year, about 93,000 of which could be eliminated by adequate prenatal and antepartum care.

The public must be educated to the point of demanding such care, and it may be used in furthering the educational program.

Practicing physicians are shirking their responsibility in prenatal and antepartum supervision, and they must assume the burden before it falls into the hands of laity-directed social service groups.

Health officers and other health workers need awakening to the opportunity for service in the campaign for the reduction of fetal, neonatal and maternal mortality.

The most practical standard of effectiveness of a program for prenatal and antepartum care at present is 100 per cent attendance either at the office of the family physician or at the prenatal and antepartum clinics.

SCHLUTZ, Chicago.

Society Transactions

PHILADELPHIA PEDIATRIC SOCIETY

Tuesday, Feb. 12, 1935

JOHN DONNELLY, M.D., *Presiding*

PSEUDOHYPERTROPHIC PROGRESSIVE MUSCULAR DYSTROPHY; PRELIMINARY REPORT ON PATIENTS TREATED WITH AMINO-ACETIC ACID. DR. LEONARD F. BENDER.

There are various types of this disease, among which it is difficult to differentiate definitely; each type is a progressive stage of the previous phase. The disease usually affects first the muscles of the lower extremities, especially the gastrocnemius muscles. Next it affects the gluteus muscles, and as it progresses it also affects the muscles of the upper half of the body and, finally, some of the face, including the orbicularis oris muscle, the disease of the latter causing typical tapir mouth.

The condition is usually limited to children of poor parents and usually begins between the sixth and tenth years of life, although cases have been reported in patients as young as 2 years of age and as old as 50 years. It is rare after puberty.

In this disease the physiology of the muscle plays an important rôle, and when muscles are unable to metabolize the substances necessary for their growth and normal function hypertrophy in some of the individual muscle fibers occurs, with proliferation of the nuclei. This is followed by atrophy, and as this is a complex degenerative process, hypertrophy and atrophy may go on in the same muscle simultaneously in conjunction with loss of the transverse striae and vacuolation, an increase in the connective tissue and fat between the muscle bundles, and beginning weakness in the muscles. There is at first true hypertrophy to compensate for this weakness, followed by pseudohypertrophy and, later, atrophy, depending on the degree of involvement of the various groups of muscles.

Milhorat, Techner and Thomas stated that the patients with this disease show creatinuria even when on a creatine-free diet, and that they excrete ingested creatine almost quantitatively (from 65 to 100 per cent of the amount ingested). The inability to retain ingested creatine, they asserted, is in proportion to the severity of the disease.

The clinical picture in an ordinary case is usually plain. A patient sitting on the floor wishes to stand. To do so he must roll over on his abdomen, rise to his knees and then pull himself up gradually by climbing on his own legs hand over hand. This condition is often referred to as Growers' sign. As he finally attains the erect position the abdomen is thrown prominently forward, producing lumbar lordosis. His tottering uncertainty proclaims a progressive weakness with marked disturbance in gait, which becomes the steppage type. The loose shoulder girdles are best demonstrated if the examiner places his hands under the axillae and tries to lift the patient. The sensation is as though an eel were slipping through one's grasp. The condition gradually becomes worse; the patient is bedridden for from four to twelve years after the beginning of the disease, death usually resulting from some contributory cause.

While 25 patients have been observed at the Philadelphia Shriners' Hospital for Crippled Children during the past six years, thus far only 8 of them have been treated with amino-acetic acid. In this series alternate patients were put on a creatine-free diet and on a diet containing 1.75 Gm. of protein per kilogram of

body weight, the remainder of the calories being furnished by fats and carbohydrates, approximately as follows: proteins, 50 Gm.; fats, 100 Gm., and carbohydrates, 150 Gm. One week after admission to the hospital the administration of amino-acetic acid was started. Five grams was given twice daily to children under 10 years of age, and 5 Gm. was given three times a day to children over 10 years of age. The same dosage was continued in the home after discharge from the hospital. Determinations of the urinary creatine and creatinine were made daily by the Folin method, and a marked rise in the output was noted from twenty-four to forty-eight hours after amino-acetic acid was started. In the milder cases this increase remained fairly constant for about two weeks; then there was a gradual return to practically the original output, which was maintained during the remainder of the stay in the hospital. The more severe the case, the higher and more variable the output, the longer the time necessary to show a decline in the output. The creatinuria is apparently not significantly altered by excessive intake of fluids or by diet or exercise. In all cases the Wassermann reaction of the blood was negative; the blood picture was normal, and the basal metabolism was low, ranging from minus 3 to minus 10. The blood pressure was normal for the age. Determinations of the chemistry of the blood cells were normal, except for a low phosphorus content. The measurements of the arms and legs at monthly intervals showed practically no change.

In the two cases described in detail the results were similar to those obtained in the other cases. Since November 1934 the new patients with this disease admitted to the hospital have been treated with amino-acetic acid administered by iontophoresis instead of by mouth. The latter method will be more fully described in the discussion. So far no definite report can be given as to the ultimate results obtained, but if the benefits are as great as those derived by the previous method it will mean an appreciable saving in the amount of amino-acetic acid needed, and as treatment must be continued over a long period to prevent relapse the cost of the amino-acetic acid, even though it has been greatly reduced in the past year, is still of paramount importance in the treatment of the disease.

DISCUSSION

DR. A. A. MARTUCCI: The important question arises: What is the disturbance in muscular dystrophies? Is it general or predominantly local? If one assumes that it is local, the local administration of amino-acetic acid should be the method of choice. This thought led my associates and me to introduce amino-acetic acid into the musculature by electrophoresis. This method insures an even distribution of amino-acetic acid and is preferable to the injection method.

Electrophoresis (iontophoresis) implies that ions are introduced into the tissue by help of the galvanic current. The technic is as follows: A saturated aqueous solution of amino-acetic acid is used. This consists of 17 Gm. of amino-acetic acid dissolved in 100 cc. of water. This quantity is sufficient for nine successive treatments. Two asbestos compresses 12 by 5 inches (30.5 by 12.7 cm.) were utilized. We have found that asbestos is more satisfactory than gauze or blotting paper, for it absorbs less fluid and keeps moist for a longer period. An asbestos compress is wrapped about each thigh, thereby making possible treatment of two regions at the same time. This is done with the help of a bifurcated cable extending from the positive pole. A large dispersive electrode is placed along the lumbar spine. The positive current is applied to both thighs; the amperage depends on the tolerance of the patient and ranges from 2 to 6 milliamperes. The duration of the first treatment is twenty minutes; this is increased ten minutes with each successive treatment until the patient is receiving a full hour of treatment. This treatment is given three times weekly. We have found that the longer the flow of current the better, for one gets a more basic induction of amino-acetic acid into the body, and furthermore the long continued galvanization has a tonic action on the affected muscles.

On removal of the asbestos electrode there may or may not be an area of erythema and gooseflesh; this, I believe, is dependent on the sensitivity of the skin

to the current and also on the strength of the current used. This erythema persists for from three to four hours following the removal of the asbestos electrode.

There has been no ill effect following any of our treatments. We have administered nearly one hundred treatments. Both objective and subjective improvement has been noted, but it is as yet too early to evaluate the results. Objective increase of strength was noted. We expect considerable regeneration of the diseased musculature as shown by slight increases in the circumference of both thighs where treatment has been applied.

Dr. Alfred Hand: I tried amino-acetic acid on the younger of two brothers with this condition; the other had died before this treatment was advocated. I also tried epinephrine hydrochloride and pilocarpine hydrochloride, given hypodermically, and then amino-actic acid. At the start I was much encouraged. The boy brightened up. He said that he did not feel tired as he used to and that he felt as though he could walk. The nurses were enthusiastic. The boy sat up for fifteen minutes. All were so favorably impressed that Dr. David Riesman asked me to take over 2 other boys. We pushed this treatment thoroughly, increasing the dose, and continued it for some months. It made the patients feel better. The first boy thought that he could move his feet a little from side to side. But he died in spite of the treatment. I think that this is not a fair trial; we do not get the patients until the disease is advanced. The treatment should be started in infancy when the disease begins, then further progress might be prevented.

Dr. Alfred Gordon: The condition described in Dr. Bender's paper is and always has been a baffling one. Physicians have contented themselves in cases of this kind simply with the statement that the case is one of muscular dystrophy. A few autopsies have shown that the muscular tissue is atrophied or disappears and that connective tissue or fat develops in its place. That is all that was known about it. As a rule, the children are brought to the physician when they are advanced in years—11, 13 or 15 years old. It was delightful to learn a few years ago that a chemist came to the rescue of physicians and spoke of creatine and creatinine and found a connection between the amount of creatine and creatinine and muscular dystrophy. Some authors who have reported cases of this disease noted the disturbance of the creatine metabolism. They believed that any agent which would dissolve the creatine would prevent the further progress of the disease. Encouraged by these reports, I undertook to treat 2 patients—one a boy of 11 years, the other a boy of 13 years—the one for six months, the other for eight months. I determined the amount of creatine and creatinine before I undertook the treatment. In order to test the value and the efficaciousness of the treatment I used no other measures. These patients happened to be children of parents of very moderate means who could not afford to buy amino-acetic acid, so I used ordinary gelatin, which contains 12 per cent amino-acetic acid. I have given these children about 75 grains (4.9 Gm.) a day in pineapple juice, orange juice or lemonade and have not used any other medication. The only thing that I insist on is that the patient avoid extra fatigue in order to preserve the remaining musculars fibers which have not yet suffered. I am glad to say that in one case I have obtained, conservatively speaking, some results. The boy of 13 shows some improvement. Formerly he was unable to run; at present he runs a little and he does not get as tired as formerly. He had difficulty in climbing stairs eight months ago. At present he can do it with a great deal of ease. The other boy, 11 years old, also shows some improvement, but not as much as the boy of 13. In treating these patients there is, therefore, at the present time something to rely on.

Another thought that occurs to me in considering the question of dystrophy is this: One frequently observes that muscular dystrophy is a familial disease. I might say that these two boys are first cousins. I have observed that the condition runs in families, occurring in one, two or several members. Very likely it is a morphologic or developmental deviation from the normal. Since it runs in families and is sometimes hereditary, I conceived the idea of beginning with treatment of the mother. Since the disease is due to a chemical disturbance in the creatine and

creatinine metabolism, why not give the mother amino-acetic acid before she becomes pregnant? One of the mothers whom I have been treating in this manner for many months is contemplating becoming pregnant. The subject remains a baffling one, because one is dealing with a morphologic condition.

DR LEONARD F. BENDER: At present amino-acetic acid is the best medicament available for this condition. As Dr. Gordon has told us, the disease is a baffling one. One hopes that with continued studies physicians may be able to stay the course of the disease and prolong the lives of children suffering from it.

EFFECT OF VACCINATION WITH BCG ON INFANT AND CHILDHOOD TYPES OF TUBERCULOSIS, WITH CORRELATION OF TUBERCULIN REACTIONS, ROENTGEN DIAGNOSIS AND MORTALITY. DR. J. D. ARONSON and DR. A. M. DANNENBERG.

Between December 1927 and October 1934, 70 children were vaccinated by the peroral administration of BCG vaccine. One hundred and sixty-seven unvaccinated children were studied as controls. Of 41 children vaccinated with BCG and exposed to persons with tuberculosis whose sputum gave positive cultures for tubercle bacilli, 1, or 2.4 per cent, died of tuberculosis, while of 84 unvaccinated children who lived under comparable conditions, 11.9 per cent died of the disease. Of 15 children vaccinated with BCG who remained in contact with persons whose sputum gave negative cultures, none died of the disease, while of 45 unvaccinated children living under comparable conditions 2, or 4.4 per cent, died of tuberculosis. Of 14 children vaccinated with BCG who were not exposed to tuberculosis and 38 unvaccinated children living under comparable conditions, none died of this disease. Of children in contact with persons whose sputum gave positive cultures, 82 per cent of those vaccinated and 79 per cent of those unvaccinated reacted positively to the intracutaneous injection of tuberculin. Among 14 vaccinated and 44 unvaccinated children in contact with persons whose sputum gave negative cultures, 93 per cent of those vaccinated and 36 per cent of those unvaccinated reacted to tuberculin. Among children not in contact with persons known to have tuberculosis, 75 per cent of those vaccinated and 24 per cent of those unvaccinated reacted to tuberculin. Of children living in contact with persons whose sputum gave positive cultures for tubercle bacilli, 17 per cent of those vaccinated with BCG and 57 per cent of the unvaccinated children presented roentgenologically demonstrable lesions of the lung. Among children living in contact with persons whose sputum gave negative cultures for tubercle bacilli no roentgenologically demonstrable lesions were observed in the vaccinated children, while 5 per cent of the unvaccinated children presented pulmonary lesions. No lesions demonstrable by means of the roentgen rays were found in the vaccinated or the unvaccinated children not in contact with persons known to have tuberculosis.

The BCG culture used in this study has remained attenuated for both man and guinea-pig when maintained according to the method described by Calmette.

DISCUSSION

DR. H. HARRIS PERLMAN: Is there any real significance in the evidence of Petroff of Saranac concerning the use of avirulent BCG?

DR. J. D. ARONSON: I believe that one should not completely disregard Petroff's early findings of the virulence of cultures of BCG, since my associates and I obtained a culture of BCG in 1926 which produced tuberculosis in guinea-pigs. Cultures which have subsequently been obtained, however, have consistently failed to produce tuberculosis in animals, even when administered in large doses. Attempts to increase the virulence of the BCG culture have failed in the hands of most investigators. The advisability of vaccinating the general population with BCG vaccine should be studied. I do not see the necessity of revaccinating children with the BCG vaccine at yearly intervals if they are in a household with a person with manifest tuberculosis, since spontaneous vaccination with the virulent bacilli occurs. Vaccination with BCG materially reduces the incidence of death from

tuberculosis, especially within the first three years of life. As to the value of the BCG vaccine in preventing tuberculosis during adolescence and adult life, further data are desirable.

TREATMENT OF HYPERTHYROIDISM IN CHILDREN AND YOUNGER ADOLESCENTS. DR. EDWARD ROSE and DR. ELIZABETH KIRK ROSE.

Hyperthyroidism in children is dealt with at some length in the literature. Most writers recommend thyroidectomy or conservative treatment with rest and iodine. The purpose of this communication is to review 10 cases of hyperthyroidism in patients under the age of 15 years in which irradiation therapy was employed and to consider the value of such therapy in juvenile hyperthyroidism. The reasons for using irradiation are reviewed in some detail. Three types of hyperthyroidism in children as observed in this region are described: first, a frank primary type; second, a frank secondary type in which symptoms are engrafted on a preexisting goiter, and, third, mild or borderline types. The differential diagnosis is discussed. The existence of iodine-induced hyperthyroidism is briefly discussed. The important clinical details of our cases are reviewed by means of lantern slides. The following points are emphasized: (1) the frequency of gain in weight after treatment, (2) the drop in the basal metabolic rate to subnormal levels after treatment, (3) the "dispersion phenomenon" and (4) the reduction in size of the thyroid after treatment. Our one fatal case is briefly described. It is concluded that properly controlled irradiation is worth a trial in juvenile thyrotoxicosis if nodular goiter is not present.

DISCUSSION

DR. EUGENE PENDERGRASS: There are a number of points brought out in this paper that might bear repetition and discussion.

I think that the important point of not removing the thyroid gland during adolescence because of its interrelation with other glandular structures is especially noteworthy. I do not believe that this has been fully appreciated and, so far as I know, it is the first time that it has been definitely stressed.

I should like to say a word about the unit of roentgen therapy, the roentgen. This unit is the same as any other standardized unit of measurement, and it can be delivered on Pike's Peak as well as on sea level, or it can be delivered in any country. It represents a distinct advance in roentgen therapy and makes it possible for one to refer patients to various physicians without danger. It also makes it possible for one to compute the dosage at various depths. This my associates and I have determined by using a water phantom. The brain, liver, thyroid and muscles have approximately the same absorption values. There is a slight variation in the lungs and small intestines, which contain air or gas.

I was impressed with Dr. Rose's statement that in the majority of patients under 45 years of age there is a tendency toward spontaneous permanent remission. If this is true, it behooves physicians to consider a treatment that is conservative.

The object of irradiation is to prevent overactivity of the gland. How this is brought about is not known at the present time, but it is known that even excessive irradiation over the normal thyroid gland does not change the basal metabolic rate. I have observed this in numerous instances in which the patient was suffering from carcinoma of some structures in the neck and large doses of high voltage therapy were applied. Apparently there is no effect on the normal thyroid, at least with the dose that is utilized in therapy.

In giving roentgen therapy my associates and I give treatment when there is elevation in the basal metabolic rate and even in the absence of elevation in the basal metabolic rate if there are clinical signs and symptoms to suggest the presence of residual toxicity. We depend a great deal on the advice of Dr. Rose as to when we should discontinue irradiation so far as the general condition of the patient is concerned. Treatment is carried to such a point that the basal metabolic rate is down below normal; otherwise a recurrence may develop.

In the past we have never promised the patient that the gland would decrease in size or that the exophthalmos would disappear. In this series of cases in the majority the gland tended to decrease in size. I have been impressed, however, with the frequency with which the exophthalmos persists, even after the patient is perfectly normal otherwise.

In the beginning one cannot tell how many treatments will be necessary. There is so much individual variation in susceptibility to irradiation therapy that one cannot say that two or four or a given number of treatments will be sufficient, but after the first two or three treatments one can gain some idea as to the susceptibility of a given patient.

In treating these patients we have always included the upper part of the chest in the portion that is being treated. It is therefore necessary to have a roentgen examination of the chest to be sure that there is no underlying tuberculous process which might be lighted up by roentgen therapy.

Along with this, one should be careful to tell the family about the falling of hair—alopecia. I have never seen this occur in children, but I have seen alopecia in adults, even though the patient was not treated, and it is extremely difficult for the radiologist to protect himself, because it is well known by physicians and by the laity that the roentgen rays will remove hair.

One distinctive advance in roentgen therapy is that with the increase of the thickness of the filter (for example, at the present time a copper filter of from 0.25 to 0.5 mm. is used) telangiectasis does not develop.

If some of our patients do not respond to the usual doses, we increase them, even treating these patients with high voltage, and it has been surprising that the results of roentgen therapy have gradually improved as we have increased the dose.

DR. JULIAN LYON: I had the privilege of reading Dr. Rose's paper before I came here. From the point of view of the pediatrician, the significance of the paper is to make known the results of treating hyperthyroidism in children by irradiation with the use of scientifically standardized doses. In other words, the doses previously used were not standardized and so not as safe by any means, as Dr. Pendergrass has said, as the present standardized doses are. In children, as was mentioned by Dr. Rose, it is especially necessary to preserve sufficient thyroid gland activity for mental and physical normal growth. In children, one cannot accomplish the same results following overtreatment as in adults. If the thyroid in adults is overtreated or if too much is removed, there is a certain amount of hypothyroidism; by the administration of thyroid this can be corrected. That correction is not so successful in children. Hyperthyroidism is not rare, but in the experience of most pediatricians it is seldom met with. Most of these patients go directly to clinics for patients with goiter. Dr. Rose has mentioned three types that he has seen in this locality: first, frank cases in which goiter and the symptoms appear about the same time; second, cases of nontoxic conditions which later become toxic, and third, borderline cases. As pediatricians we have to recognize these types and decide whether to use conservative treatment or to refer the patient to the roentgen department for irradiation or to the surgeon for surgical treatment. Conservative treatment consists in mental and physical rest, and a high caloric diet. This takes weeks or months. Some patients who have a mild illness in the beginning do not remain mildly ill. The jump from this conservative treatment to thyroidectomy has been a great one. The standardization of the dosage of radiation in competent radiologic departments should be of great value to those who do not improve spontaneously but who tend to get a little worse. From the teaching of Dr. Means, I have come to think of the use of iodine as a preoperative aid, and I do not think that it stops hyperthyroidism. It does reduce its intensity. It has much the same relation to hyperthyroidism that salicylates have to rheumatism—it serves to reduce the symptoms but not to stop the activity of the disease. For preoperative use my associates and I have found that the administration of iodine for a period of from eight to ten days previous to operation reduces nervousness and metabolic activity in children. In regard to basal meta-

bolic studies in children, the results that one gets with metabolic tests on children, especially at puberty, are not as satisfactory as they are for adults.

In regard to focal infection in children with hyperthyroidism, the question arises whether or not to treat the diseased tonsils or adenoids, diseased sinuses or teeth before or after special treatment of the thyroid condition. In some children, e. g., those at Lahey's Clinic in Boston, when they are prepared for operation thyroid treatment is begun at once, and focal infection is treated later.

As to the selection of patients for treatment, I suspect from what Dr. Rose has said about the selection of these patients, especially those with fatal conditions whom he was about to speak of but did not, that the patients who appear obviously very toxic at the start are not accepted for irradiation treatment. These patients are probably better referred directly for surgical treatment because this properly carried out is successful. Dr. Lahey claims that operations on the thyroid done in a clinic where this form of surgical intervention is constantly practiced are much better than those done in hospitals where such operations are only occasionally performed.

Dr. Edward Rose: It might be of some interest to review briefly the features of our fatal case. In the beginning, this girl, who was 14 years old, did not look particularly different from several of the other patients who did well under treatment. She had had symptoms for about nine months. She had received three separate courses of iodinization. The basal metabolic rate was plus 45 per cent. As I said, she showed a temporary moderate improvement, with a drop in her basal rate to plus 24 per cent within about a month; following that her symptoms increased. From the middle of August to the middle of October we did not see this girl. When we finally saw her, in the middle of October, she was desperately sick with advanced congestive heart failure. We referred her at once to the medical division for the purpose of preparing her for operation, but four days later she suddenly died of congestive heart failure. We were unable to obtain permission for an autopsy. The condition was certainly some kind of acute heart failure.

We are obviously to blame for this girl's death, and yet we believe that part of the blame rests on the radiologist. If we had seen this girl between August and October and had seen the evidence of congestive heart failure, we could have had her successfully operated on. One item serves to point a moral: She had received three courses of iodinization before she came to us. The rules against the treatment of hyperthyroidism with iodine are practically the same in children as they are in adults. I am sure that all the members know that to attempt to treat a patient with iodine is, in about 96 per cent of cases, a serious mistake. Only a certain amount of benefit is to be derived; the patient is apt to become iodine-fast, and one has lost one of the most valuable tools. The same thing applies to a slightly lesser degree in children. Iodine should be reserved for treatment of thyrotoxic crises, for preoperative use and, in a few cases, as an aid to diagnosis when the differential diagnosis is extremely difficult.

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Dec. 17, 1935

Abraham Levinson, M.D., *President, Presiding*

Persistent Sinus Tachycardia. Dr. Gustave F. Weinfeld.

S. L., an Italian girl, aged 12 years, was admitted to the pediatric department of the Research and Educational Hospital of the University of Illinois for study in May 1930. She complained of palpitation and faintness and was known to have had a rapid pulse rate for many months. The exact duration of these

disorders was unknown. No other relevant points were elicited in the history except that she had had occasional vague and fleeting pains in her knees and that her tonsils had been removed when she was 8 years old.

Physical examination revealed a well nourished preadolescent girl. The secondary sex characteristics were not developed. Cardiac findings were negative except for tachycardia in which the rate varied between 150 and 172. Her color was good, and her respirations were of normal rate and depth before and after exertion. There was profuse perspiration, particularly of the axillae and hands. There was a slight tremor of the fingers. The thyroid was not palpable, and the eyes were not prominent.

During hospitalization the pulse rate varied between 100 and 150. No rates were taken during sleep, but the patient was extremely cooperative and seemed to be completely composed during all the observations. Her temperature remained at a normal level, and her blood pressure varied between 110 systolic and 60 diastolic and 120 systolic and 70 diastolic.

Cytologic and chemical studies of the blood gave negative results. Repeated urinalyses and kidney function tests showed no abnormality. The basal metabolic rate was +17 per cent on one occasion and +18 per cent on another. The curve for sugar tolerance was normal. She had a very faint reaction to an intradermal injection of 0.1 mg. of old tuberculin. A roentgenogram of the chest revealed a heart of normal size and an old healed tubercle. Her response to the Goetsch test suggested sympathicotonia, but this was not conclusive because the acceleration of the pulse rate which followed the administration of epinephrine was not associated with an elevation of the blood pressure.

She was discharged from the hospital three weeks after admission and was kept at absolute rest in bed for a period of four months. Thereafter her activity was partially restricted for two more months. She has received increasing doses of compound solution of iodine up to as much as 50 drops a day, without noticeable effect on the clinical picture. Since the tachycardia did not subside during this prolonged period of observation, it was decided that she be permitted to return to school and that no restriction whatever be placed on her activity.

She has always gained weight steadily but showed a definite spurt when the secondary sex characteristics first appeared, and this marked increment in weight continued for several months after menstruation began. The tremor and hyperhydrosis have gradually diminished without any apparent relation to the sexual development. Preceding menstruation the pulse rate varied between 150 and 160; at present it averages about 140; it has always shown the usual responses to exercise and changes in position. The last recorded blood pressure was 112 systolic and 82 diastolic, which was slightly lower than the usual readings.

Eleven basal metabolism tests have been made over a period of four and a half years. The rates have varied from +8 to +35 per cent. The last rate recorded was +10 per cent.

All electrocardiograms have shown the tachycardia to be of a simple variety. The rhythm is regular, and the characteristics of the P waves indicate that there are no abnormalities of the pacemaker. In one curve we induced an auricular-ventricular block by ocular pressure, thus demonstrating responsive vagal activity.

In attempting to explain the etiology and nature of this condition it is necessary to consider first the more common and obvious causes of persistent tachycardia. Active infection, anemia and cardiac pathologic changes can be excluded as possible causes, since confirmatory evidence of these conditions never appeared. Hyperthyroidism, which is rare in childhood, was suggested to us early in the course of our observations, but the absence of the cardinal symptom of loss of weight rendered this diagnosis inapplicable.

The influence of the endocrine glands on cardiac activity is known to be important. This is particularly striking in certain types of young girls who show a reaction at puberty consisting of evidences of vasomotor instability, increased metabolism and tachycardia. These signs appear shortly before puberty is established and disappear not long thereafter. Our patient presented signs more or

less typical of the puberty reaction, but as the tachycardia has persisted for two years since menstruation became well established the signs cannot be considered as belonging to this group.

The autonomic nervous system unquestionably plays an important rôle in the control of the heart rate. The adjustment between the antagonistic sympathetic and parasympathetic systems is delicate. When this adjustment is "out of kilter" innumerable combinations of symptoms may occur, for overactivity or depression of one or the other system may vary in different segments of the body. It is difficult, therefore, to establish in any case a clearcut diagnosis of parasympatheticotonia or sympatheticotonia.

If this case has any teaching value at all it lies in the lesson that certain types of tachycardia, even though extreme, may be benign. Any one seeing this child for the first time might institute a regimen of absolute rest or at least curtailed activity. The proof that such a program is unnecessary in this case and that this child has been spared the unfortunate psychologic reaction which so many cardiac cripples have, lies in the picture of health and happiness which she presents at the present time.

SPONTANEOUS TENSION PNEUMOTHORAX IN A FOUR YEAR OLD GIRL. DR. H. W. ELGHAMMER.

Collection of air under pressure in the plural cavity suggests not only a break in the continuity of the visceral pleura but also the presence of a valve mechanism which allows the air to enter but prevents its escape.

Although this condition is referred to as spontaneous, one finds in many instances some previous pathologic change which may predispose to or actually cause this accidental condition.

A girl, aged 4 years, was brought to the office on Feb. 5, 1935, because of shortness of breath, inability to assume the reclining position, failing appetite and loss of weight. The mother stated that the condition dated back about three weeks. The symptoms had become more marked up to the last few days, when the child was unable to sleep except in the sitting position.

The patient's infancy had been uneventful, and development had been normal. During the summer of 1933, at the age of 2 years, she had bronchial pneumonia, with good recovery. In July 1934 she had a severe attack of lobar pneumonia complicated early by empyema which was treated by open drainage; complete recovery followed in five weeks. Fluoroscopic examination at this time showed normal pulmonary and cardiac findings except for thickening of the pleura over the lower and middle portions of the left lung.

Physical examination revealed a fairly well nourished girl with rather fast and shallow breathing. The whole chest seemed fixed in the position of deep inspiration, the left side definitely bulging. The skin appeared pale. No cyanosis was present except on exertion or on the attempt to assume the reclining position. The physical signs were essentially limited to the chest. The entire left side of the thorax both anteriorly and posteriorly was hyperresonant, with complete absence of breath sounds. Normal vesicular breathing was heard over the right side of the thorax. The heart was faintly audible posteriorly and to the right. The temperature was 99.2 F. taken rectally. The blood and urine were normal. Fluoroscopic examination confirmed the physical findings, showing complete pneumothorax on the left, with compression of the lower lobe of the left lung and displacement of the heart to the right and posteriorly. Stereoscopic roentgenograms taken the following day showed further a herniation of the upper lobe of the left lung into the right side of the thorax, marked displacement of the trachea, and widening of the left intercostal spaces. The tuberculin reaction was negative. These findings prompted a diagnosis of tension pneumothorax. The child had been in good health since September 1934, following the lobar pneumonia and empyema, and the lungs had been found normal except for a thickening pleura. On further questioning, the mother stated that the girl had had two severe spells of coughing one week

apart in November. The production of the pneumothorax may be explained on the basis of the existence of some adhesion between the wall of the chest and the visceral pleura and the assumption that the violent coughing had produced a tear in the lung, allowing air to enter the pleural cavity. Gradually, through some valve action, tension pneumothorax progressed to the extent seen when the child was presented for examination.

The child was removed to the hospital, and on fluoroscopic guidance a small trocar connected to a reversed pneumothorax apparatus and manometer was introduced into the fourth interspace outside the left nipple line. The interpleural pressure registered 48 mm. of mercury. Suction was applied for two minutes, and after five minutes the pressure had fallen to 22 mm. of mercury. The child was greatly relieved and was able to sleep lying down for several nights, but her difficulty soon returned. Aspiration was again carried out on Feb. 23, 1935, and the interpleural pressure at this time was 42 mm. of mercury. A roentgenogram was similar to the previous one.

It was decided to aspirate at frequent intervals in order to keep the interpleural pressure at the low level, with the hope that the damage in the lung would heal. This was done at the patient's home during a period of four months. A total of twenty-one aspirations were carried out at intervals varying from two to five days. At the time of the sixteenth aspiration the pressure was found to be negative, but the following aspiration again showed a positive interpleural pressure. The twentieth and twenty-first aspirations both showed a sustained negative pressure.

DISCUSSION

Dr. Joseph Brennemann: This is an extremely interesting case. I have for many years looked for a case of simple spontaneous pneumothorax but cannot recall ever having found one. One reads about such cases in the literature, but I think that my associates and I have never observed one. We have, on the other hand, observed many cases of pyopneumothorax.

I wonder what the possible connection was between the spontaneous pneumothorax in this case and the empyema that preceded it. We observed a child with localized empyema under pressure. Before we decided to drain it, because we are rather conservative, it broke. We allowed the boy to go home when the condition was nearly cleared up. After a time and during a period of from four to five months the pneumothorax cavity gradually increased in size until the boy became cyanotic and looked as though he would not recover unless we did something for him. He recovered after drainage was instituted. I wonder whether there might be some connection of that sort in this case. Another point: If a pneumothorax cavity increases in size we believe that there is a valvelike action of some sort. We have always wondered what one ought to do in such a case, and we thought that aspiration did no good. In this case of Dr. Elghammer's it cured the condition, but we have always believed that the amount of air that we withdrew would quickly be replaced through the valvelike action. Although we usually treat the condition first with closed drainage and after a time institute open drainage, it has always seemed to me perfectly logical to resort to open drainage at once. In doing so one is simply replacing tension pneumothorax with pneumothorax that follows open drainage and is not under tension.

Dr. Arthur H. Parmelee: The great similarity in the films of Dr. Elghammer's case to those obtained in the case of a balloon cyst of the lung which Dr. Apfelbach and I reported interests me. If the films are examined some differences are to be seen. In the roentgenograms of the balloon cyst of the lung one can see the outline of the pleural sac enclosing the air, whereas in the roentgenograms in this case air fills the whole left side of the thoracic cavity, and the air is evidently between the visceral and parietal pleura. Unless this difference is noted carefully, these two disorders could be easily confused. The first picture that Dr. Elghammer showed could almost be superimposed on the picture in our case without showing any differences except that the margins of the pleura indicate that the

air is within the pleural sac in one case and not in the pleural sac in the other. In that particular case of balloon cyst of the lung we were able to demonstrate at postmortem examination a bronchial radicle which opened into the sac in a sort of oblique position and to show that there probably was a definite valve action. I think that the mechanism in cases of balloon cyst of the lung is probably the same as in this case.

HEMATOCOLPOS DUE TO IMPERFORATE HYMEN. DR. JOSEPH K. CALVIN and DR. SAMUEL NICHAMIN (by invitation).

This article will appear in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

Book Reviews

Growing Superior Children. By I. Newton Kugelmass, M.D. Price, $3.50. Pp. 535, with 54 illustrations. New York: D. Appleton-Century Company, Inc., 1935.

There are four parts to this volume, the first entitled "Our Newborns" (covering events from conception through early infancy); the second, "Our Infants"; the third, "Our Children," and the fourth, "Our Adolescents." Individual chapters under each part deal under varying titles with growth (physical and mental), the physician's evaluation, feeding, training, behavior and the prevention of disturbances.

The book is well printed and edited and, on the whole, well written, many subjects being exceedingly well presented, but the text is at times lengthy and repetitive. The directions for proper care are given in great detail, but the author fails to distinguish between essentials and nonessentials. The routine suggested often seems unnecessarily complicated, time-consuming and expensive. Few mothers could follow it explicitly, and the selection of the items which must not be neglected would be most difficult.

The principal thesis of this volume is that by following directions given by a competent physician one can produce superior children, but that these directions must be frequently adjusted and care must be individualized, because the child is constantly changing and no two children are alike in characteristics or needs. So far as the term superior is used to mean more healthy and able than if neglected, the thesis is justified and worth emphasis, but Kugelmass unfortunately carries the concept of attainable superiority too far. To quote: "By superior home care from birth, early development can be accelerated two to three years." The implication is that without adequate medical supervision one is doomed to have inferior children but that with sufficiently frequent, thorough and intelligent supervision one can be almost certain to have superior children. The "doctrine of individuality" is constantly emphasized and possibly constitutes the most valuable educational feature of the book, but in spite of this the author tells mothers explicitly how they should care for their children and how they may successfully cope with most problems.

The purpose of this book seems good, but expresses much wishful thinking; it often tells the reader what he would like to read rather than adhering strictly to fact. Parents will undoubtedly like to read it, unless possibly they find it too long and overwhelming. The photographic illustrations are excellent, always suggesting health, vigor and happiness of the child, for which every parent yearns. The promise that their children can attain these is unmistakable, "if" they have not conceived without taking thought and "if" they have not neglected the merest detail throughout the twenty years to maturity. These oft-repeated "ifs," however, will undoubtedly strike terror in many hearts and bring frustration to any one unfortunate enough to be unable to pay for the close and detailed medical supervision suggested.

It has been implied that strict adherence to scientific fact or at least to the accepted medical opinion, when facts are lacking, has not been followed by the author. This is a serious charge and should be demonstrated by a few direct quotations.

In the section on favorable conception one reads: "The degree of emotional devotion of one parent to the other is reflected dominantly in the transmission of more vital elements in the constitution of the progeny . . . The more female the

faher's body-build, the more likely the conception of a girl." In the section on the prevention of potential disease prenatally one reads: "If hemorrhagic disease (bleeding) prevails in the family, the mother is put on a dietary which is excessively high in protein and fats." And again: "Cyclonic shocks have been observed to have preceded the birth of babies with cleft palates in Maine, with open spines in Vermont, and with genital defects in the Northwest. The least proportion of malformations at birth occurs in the Southern states where the climate is equable." Under "Prenatal Nutrition" one reads that there are forty nutrients necessary for life and that milk, butter and lettuce are "superior food sources of vitamin D." Finally, in the section on the prevention of infections the following unqualified statements appear: "All types of rheumatic disease are the result of one offending germ, the streptococcus hemolyticus . . . Successful immunization against infantile paralysis is now possible . . . Its duration is so far undetermined . . . The course of the disease can be checked by early diagnosis through spinal puncture. Then the injection of convalescent serum into the spine and into the child's veins aborts the disease and prevents paralysis." These and innumerable other statements like them seem particularly unfortunate, because the volume had such an opportunity to accomplish the author's purpose within the realm of reality.

Taken as a whole, "Growing Superior Children" impresses the reviewer as being a most unfortunate publication. Although it represents a colossal amount of work and has many features of merit and although it will undoubtedly lead many readers to seek health advice and give better care to their children, its lack of scientific restraint and its unjustified promises will unquestionably lead to the popularization of many misconceptions and cause much anxiety and disillusionment.

Glands and Efficient Behavior. By Dr. Florence Mateer. Price, $2.50. Pp. 237. New York: D. Appleton-Century Company, Inc., 1935.

The author is a psychologist who has observed glandular therapy by physicians and checked the results by mental tests and careful observation by herself and teachers who did not know the time or extent of therapy. The first chapter deals with mental capacity, largely as determined by mental tests, and discusses the relationship of inefficiency to glandular disturbances.

The greater part of the book describes patients—normal and subnormal—with thyroid, parathyroid, calcium and pituitary dysfunction. Mental sluggishness and obscure mental difficulties, with a low metabolic rate, indicate hypothyroidism. Lack of concentration, irritability, restlessness, tapping the feet, tearing the clothes, twitching and jerking and tantrums are symptoms of calcium deficiency. This condition is corrected by calcium therapy, although sometimes this must be supplemented by parathyroid therapy. "Recent studies have shown that a very large proportion of children and adolescents with behavior problems are cases that at least have a concomitant pituitary disturbance." Some persons have a multiple glandular disturbance. The final chapter points out that in many cases mongolism can be improved by glandular therapy.

The author describes many cases of patients whose intelligence quotients increased from a few to 78 points under treatment. Many children presenting serious behavior problems were cured.

This book was written for the laity. The glandular preparations used and the dosages are not included. Apparently all the medicines were given by mouth. The case histories prove that the author has obtained good results. In all except the group with thyroid disturbance one cannot but wonder what part of the improvement was due to the glandular therapy and what part to the psychologic aspects of the treatment. The material is presented in an extremely interesting manner.

Speech in Childhood. By Dr. George Seth and Dr. Douglas Guthrie. Price, $3.50. Pp. 217, with 46 illustrations. London: Oxford University Press, 1935.

Among physicians generally and even in the specialties chiefly concerned there is little scientific knowledge of speech and its defects. This well planned and not too ponderous volume contains much fundamental and interesting information on the subject

The physiology of speech, including the mechanism of production of the various phonetic sounds, is considered at some length. The development of speech and the acquisition of speech by the infant are discussed, along with the psychologic aspects. The relation of speech to the central nervous system and to hearing is explained. This groundwork makes the exposition of defects of speech easily understood.

Some physicians may find the chapters on the psychologic aspects not so easily read, though they may consider some purely medical presentations rather elementary; but the dual authorship of an otolaryngologist and a psychologist and educator has provided a well balanced volume.

In the discussions of speech as a social implement, of the first grasp by the infant of the significance of vocal sounds, of the interactions of speech and personality and like subjects the physician will find much broadening and useful information. The volume answers many questions asked of the pediatrician and directs him toward the correction of physical disabilities and maladjustments which are important factors in some disturbances, notably, stammering.

A description of the various defects is given and the method of cure outlined.

Some conclusions might be questioned, but on the whole the book is well written, judicial with due regard to conflicting views and a fair and interesting presentation of a neglected subject.

Estudio Radiologico de la neumonia en los niños. By Dr. Hector C. Bazzano. Paper. Publicationes del departmento cientifico de salud pública, serie 1, número 15. Pp. 37, with 69 plates on 16 pages. Montevideo: 1935.

Bazzano suspends the child in a special cloth bolster, which allows one to make exceptionally clear roentgenograms of the thorax. He illustrates all types of pneumonia with both anterior-posterior and transverse views, which together give an excellent idea of the process. Cavities that are doubtful in an anterior-posterior view, are plainly shown in this method by a transverse view. The book is in Spanish, but this should not deter the reader, for roentgenograms are universal when they are well done.

La diphtérie maligne. By R. Poinso. Paper. Price, 18 francs. Pp. 112, with 13 illustrations. Paris: Masson & Cie, 1935.

This small volume is one of the series on practical medicine and surgery. It contains a discussion of the history, pathologic features, symptoms, diagnosis, prognosis and treatment of diphtheria. The subject is handled briefly but completely. Of special interest is the chapter on complications. Nothing new is added to the subject of treatment.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Heereplein, Groningen, The Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

FOREIGN

British Paediatric Association

President: Dr. Hugh Thursfield, 84, Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31 A, Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1, Wimpole St., London. Time: Fourth Friday of each month, 4: 30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Horton R. Casparis, Vanderbilt University Hospital, Nashville Tenn.
Secretary: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Place: Kansas City, Mo. Time: May 11-15, 1936.

American Academy of Pediatrics

President: Dr. Henry Dietrich, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Region II. Place: Baltimore. Time: Nov. 16 and 17, 1936.
Region III. Place: Cincinnati. Time: Nov. 20 and 21, 1936.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

American Pediatric Society

President: Dr. Fritz B. Talbot, 270 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Bolton Landing, N. Y. Time: June 11-13, 1936.

Canadian Society for the Study of Diseases of Children

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.
Place: Bolton Landing, N. Y. Time: June 11-13, 1936.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. C. F. McKhann, Children's Hospital, Boston.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. L. Howard Smith, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Morris Bridgeman, Children's Clinic, Portland, Ore.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON PEDIATRICS

Chairman: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. Morgan Smith, 625 Beech St., Little Rock.
Secretary: Dr. Madeline A. M. Melson, 2111 N. Spruce St., Little Rock.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. S. J. McClendon, 2001 Fourth Ave., San Diego.
Secretary: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Place: Coronado. Time: May 25-28, 1936.

GEORGIA PEDIATRIC SOCIETY

President: Dr. William Willis Anderson, 478 Peachtree St., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta, December 1935. Savannah, June 1936.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. Milo K. Miller, 122 N. Lafayette Blvd., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Charles James Bloom, 3439 Prytania St., New Orleans.
Secretary-Treasurer: Dr. J. A. Crawford, 834 Ryan St., Lake Charles.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.
Place: New York City. Time: April 27-29, 1936.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. R. E. Wilson, 205 S. Harvey St., Greenville.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. J. R. Ashe, 306 N. Tryon St., Charlotte.
Secretary: Dr. R. A. Moore, 306 N. Tryon St., Charlotte.
Place: Pinehurst. Time: May 6, 1936.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

PENNSYLVANIA MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Joseph Stokes, Children's Hospital, Philadelphia.
Secretary: Dr. Theodore O. Elterich, 310 Medical Arts Bldg., Pittsburgh.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. William Weston Jr., 1428 Lady St., Columbia.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Memphis. Time: April 1936.

TEXAS PEDIATRIC SOCIETY

President: Dr. C. O. Terrell, 813 Medical Arts Bldg., Fort Worth.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

ACADEMY OF MEDICINE, TORONTO, SECTION OF PEDIATRICS

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

BRONX PEDIATRIC SOCIETY

President: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Secretary: Dr. Samuel Tripler, 1555 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Thurman B. Givan, 115 Remson St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. A. Levinson, 30 N. Michigan Ave., Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month.

Dallas Pediatric Society

President: Dr. I. T. Nesbitt, 1719 Pacific Ave., Dallas, Texas.
Secretary: Dr. John E. Ashby, 614 Medical Arts Bldg., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Harris County Pediatric Society

President: Dr. Byron P. York, 3820 Fannin St., Houston, Texas.
Secretary-Treasurer: Dr. E. O. Fitch, 3717 Main St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. H. W. Brayton, 179 Allyn St., Hartford.
Secretary: Dr. Ernest Caulfield, 683 Asylum Ave., Hartford.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1103 Grand Ave., Kansas City.
Secretary: Dr. S. A. Stadler, 6133 Brookside Blvd., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. George P. Laton, 1136 W. 6th St.
Secretary-Treasurer: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Charles F. Fisher, 756 Eastern Parkway, Brooklyn.
Secretary: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144, 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

Milwaukee Pediatric Society

President: Dr. J. Gurney Taylor, 324 E. Wisconsin St., Milwaukee.
Secretary: Dr. H. B. Miner, 425 E. Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Béla Schick, 17 E. 84th St., New York.
Secretary: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.
Secretary: Dr. A. V. Stoesser, University Hospital, Minneapolis.

Philadelphia Pediatric Society

President: Dr. H. H. Perlman, 1904 N. Franklin St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. George J. Feldstein, 3401 5th Ave., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Tuesday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Samuel A. Anderson Jr., 2326 W. Grace St., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. J. V. Cooke, St. Louis Children's Hospital, St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Arthur E. Wade, 1215, 4th Ave., Seattle.
Secretary: Dr. Walter B. Seelye, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Samuel Levin, 2501 W. Grand Blvd., Detroit.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, Oct., Dec., Feb. and April.